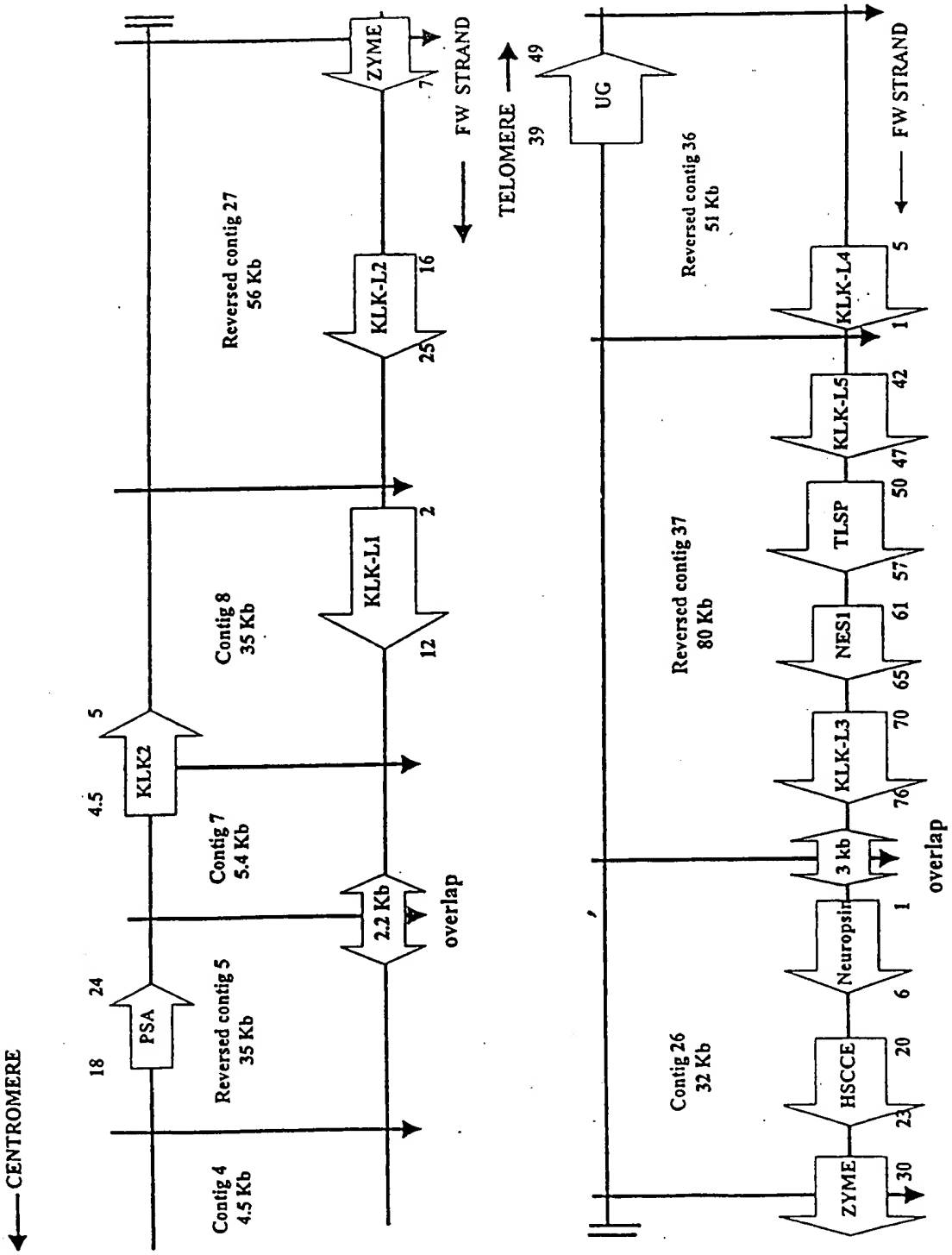
FIGURE 1


CENTROMERE
Contig 4
4.5 Kb
Reversed contig 5
35 Kb
PSA
18
24
Contig 7
5.4 Kb
KLK2
4.5
5
Contig 8
35 Kb
2.2 Kb
overlap
KLK-L1
12
2
Reversed contig 27
56 Kb
KLK-L2
25
16
ZYME
7
FW STRAND
TELOMERE
Contig 26
32 Kb
Reversed contig 37
80 Kb
Reversed contig 36
51 Kb
UG
39
49
Neuropsin
6
1
3 kb
overlap
HSCCE
20
23
ZYME
30
KLK-L3
70
76
NES1
61
65
TLSP
57
50
KLK-L5
42
47
KLK-L4
1
5
FW STRAND

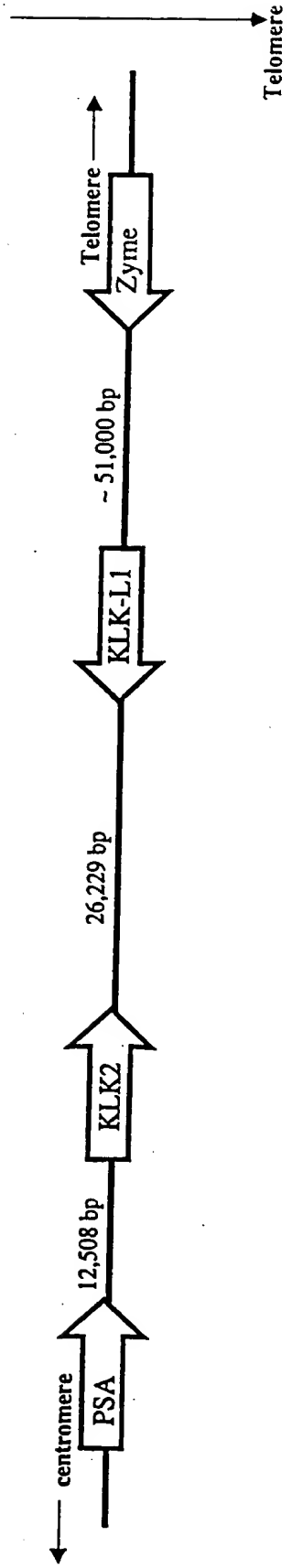

Telomere
Telomere
Zyme
~ 51,000 bp
KLK-L1
26,229 bp
KLK2
12,508 bp
PSA
centromere

FIGURE 2

FIGURE 3

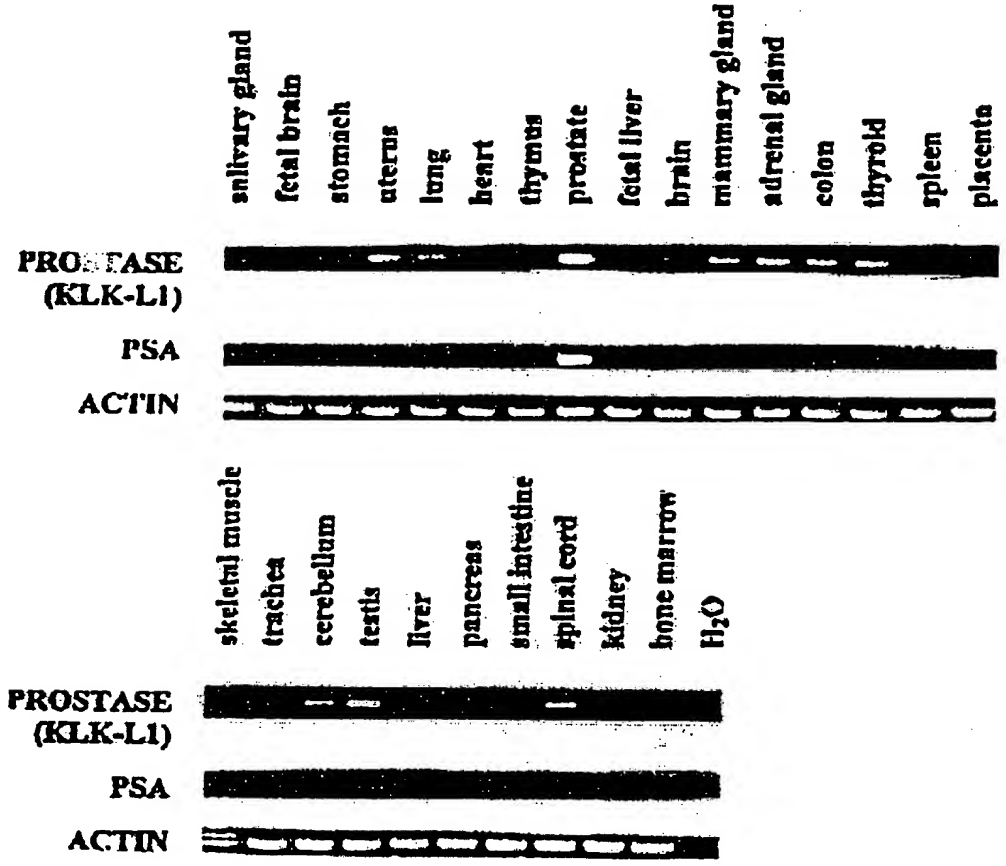

salivary gland
fetal brain
stomach
uterus
lung
heart
thymus
prostate
fetal liver
brain
mammary gland
adrenal gland
colon
thyroid
spleen
placenta
PROSTASE (KLK-L1)
PSA
ACTIN
skeletal muscle
trachea
cerebellum
testis
liver
pancreas
small intestine
spinal cord
kidney
bone marrow
H2O
PROSTASE (KLK-L1)
PSA
ACTIN

FIGURE 4

TGACCCGCTG TACCACCCCA GCATGTTCTG CGCCGGCGGA GGGCAAGACC
AGAAGGACTC CTGCAACGGT GACTCTGGGG GGCCCCTGAT CTGCAACGGG
TACTTGCAGG GCCTTGTGTC TTTCGGAAAA GCCCCGTGTG GCCAAGTTGG
CGTGCCAGGT GCCTACACCA ACCTCTGCAA ATTCACTGAG TGGATAGAGA
AAACCGTCCA GGCCAGTTAA CTCTGGGGAC TGGGAACCCA TGAAATTGAC
CCCCAAATAC ATCCTGCGGA AGGAATTC

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FIGURE 5

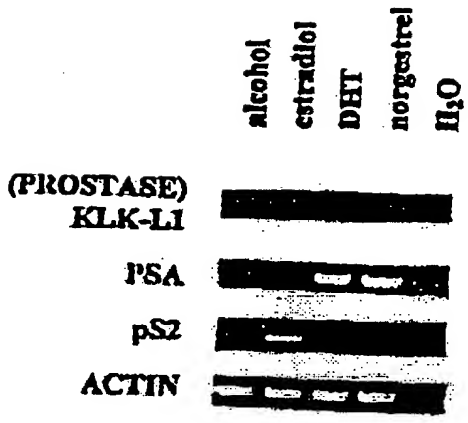

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FIGURE 6

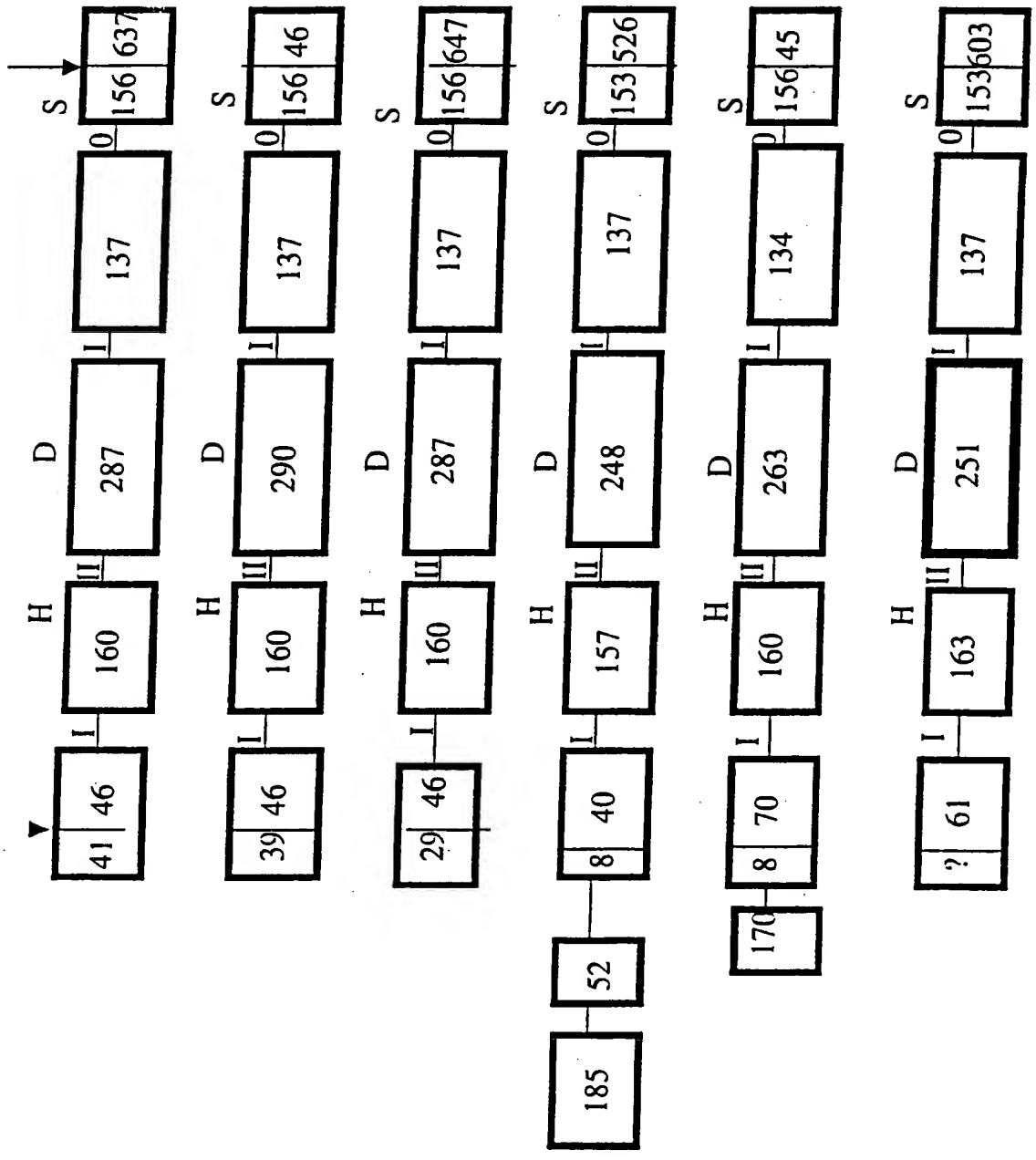
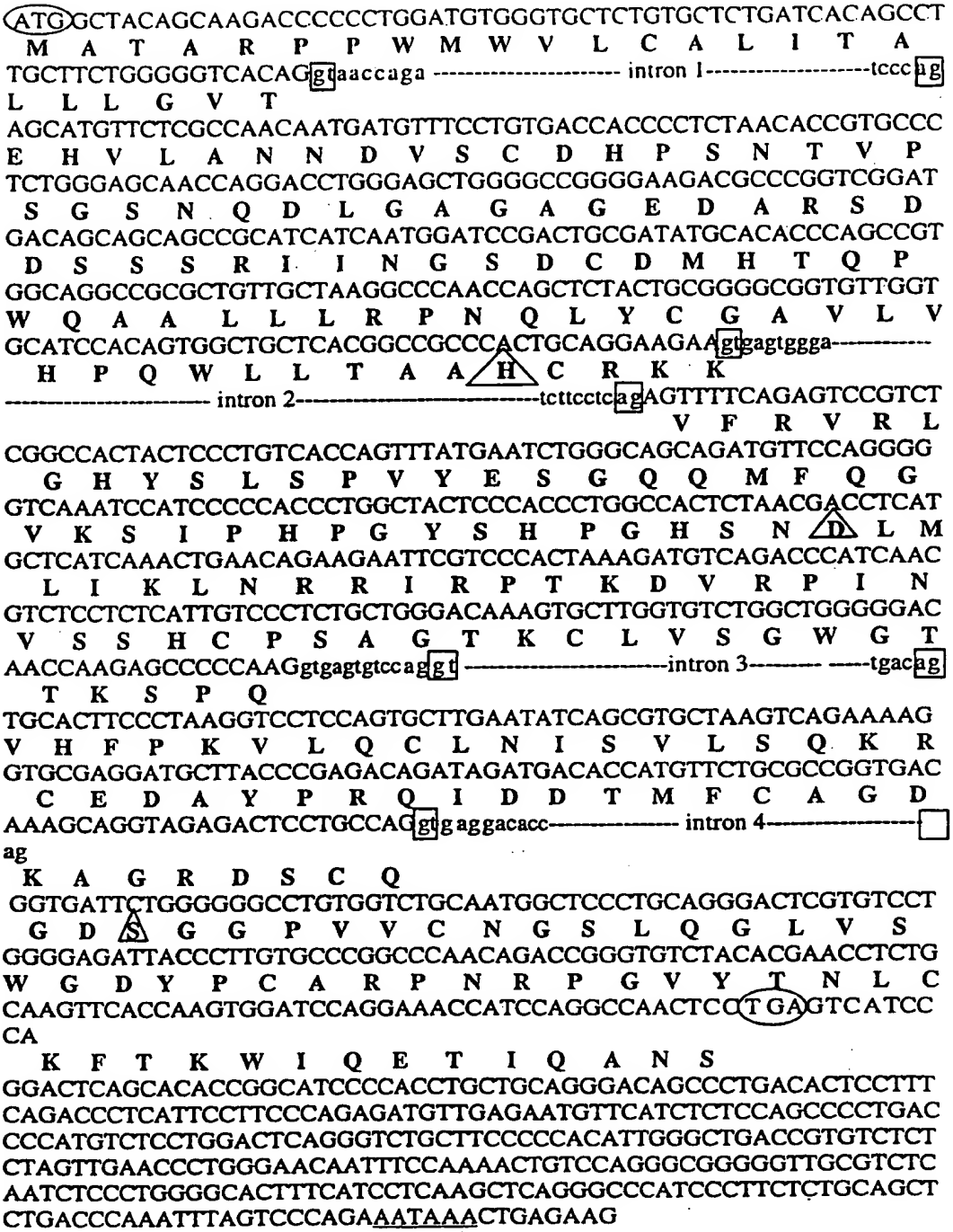


FIGURE 7


ATG GCTACAGCAAGACCCCCCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCT
M A T A R P P W M W V L C A L I T A
TGCTTCTGGGGGTCACAGgtaaccaga ---------- intron 1 ----------tcccag
L L L G V T
AGCATGTTCTCGCCAACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCC
E H V L A N N D V S C D H P S N T V P
TCTGGGAGCAACCAGGACCTGGGAGCTGGGGCCGGGGAAGACGCCCGGTCGGAT
S G S N Q D L G A G A G E D A R S D
GACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGCACACCCAGCCGT
D S S S R I I N G S D C D M H T Q P
GGCAGGCCGCGCTGTTGCTAAGGCCCAACCAGCTCTACTGCGGGGCGGTGTTGGT
W Q A A L L L R P N Q L Y C G A V L V
GCATCCACAGTGGCTGCTCACGGCCGCCCACTGCAGGAAGAAgtgagtggga----------
H P Q W L L T A A H C R K K
---------- intron 2 ----------tcttcctcagAGTTTTCAGAGTCCGTCT
V F R V R L
CGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGCAGCAGATGTTCCAGGGG
G H Y S L S P V Y E S G Q Q M F Q G
GTCAAATCCATCCCCCACCCTGGCTACTCCCACCCTGGCCACTCTAACGACCTCAT
V K S I P H P G Y S H P G H S N D L M
GCTCATCAAACTGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCATCAAC
L I K L N R R I R P T K D V R P I N
GTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGAC
V S S H C P S A G T K C L V S G W G T
AACCAAGAGCCCCCAAGgtgagtgtccaggt ---------- intron 3 -------- -----tgacag
T K S P Q
TGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGTCAGAAAAG
V H F P K V L Q C L N I S V L S Q K R
GTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGAC
C E D A Y P R Q I D D T M F C A G D
AAAGCAGGTAGAGACTCCTGCCAGgtgaggacacc---------- intron 4----------
ag
K A G R D S C Q
GGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCCTGCAGGGACTCGTGTCCT
G D S G G P V V C N G S L Q G L V S
GGGGAGATTACCCTTGTGCCCGGCCCAACAGACCGGGTGTCTACACGAACCTCTG
W G D Y P C A R P N R P G V Y T N L C
CAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCATCC
CA
K F T K W I Q E T I Q A N S
GGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTT
CAGACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTCATCTCTCCAGCCCCTGAC
CCCATGTCTCCTGGACTCAGGGTCTGCTTCCCCCACATTGGGCTGACCGTGTCTCT
CTAGTTGAACCCTGGGAACAATTTCCAAAACTGTCCAGGGCGGGGGTTGCGTCTC
AATCTCCCTGGGGCACTTTCATCCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCT
CTGACCCAAATTTAGTCCCAGAAATAAACTGAGAAG

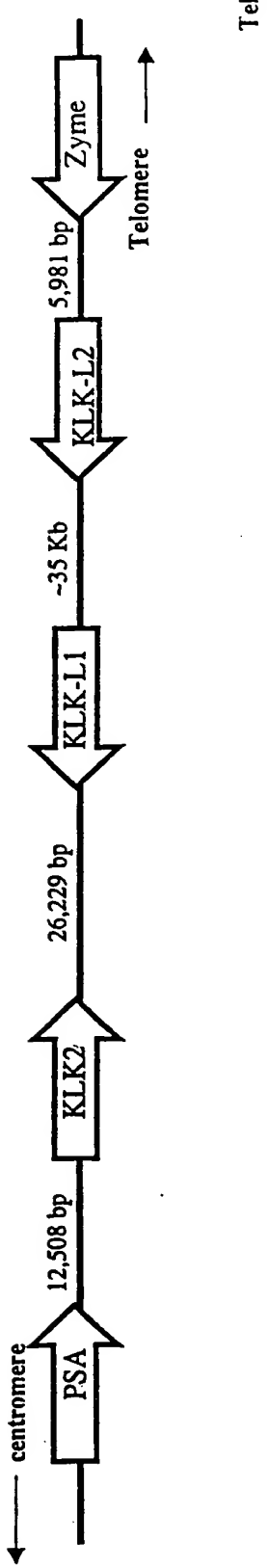

Telomere
Zyme
Telomere
5,981 bp
KLK-L2
~35 Kb
KLK-L1
26,229 bp
KLK2
12,508 bp
PSA
centromere

FIGURE 8

FIGURE 9

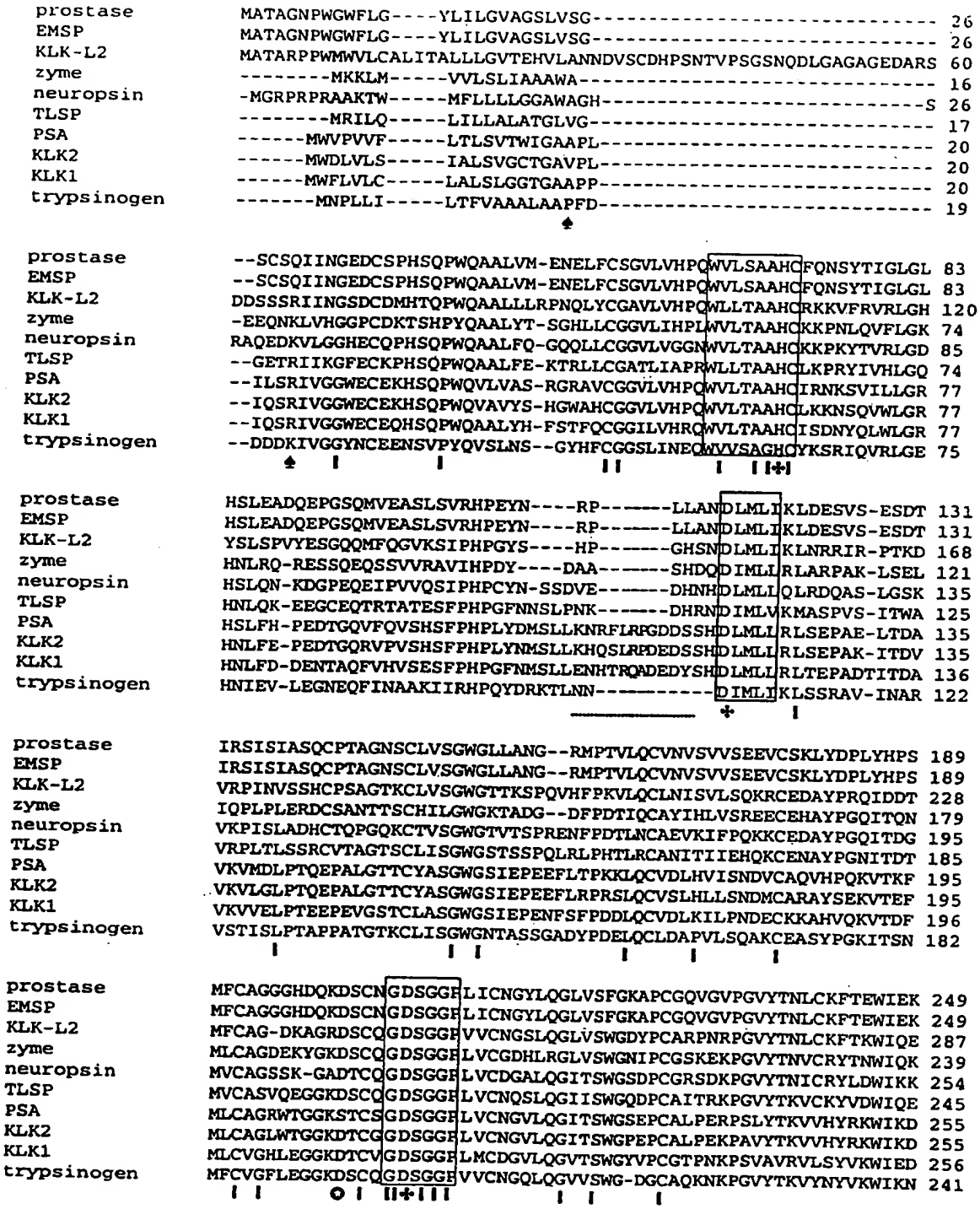
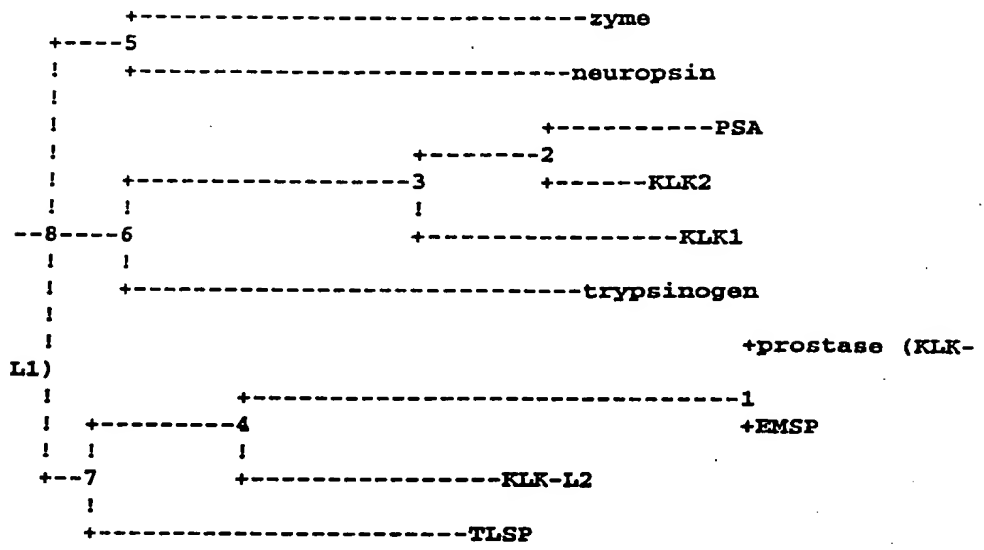

prostase
EMSP
KLK-L2
zyme
neuropsin
TLSP
PSA
KLK2
KLK1
trypsinogen

FIGURE 10

(A)


zyme
5
neuropsin
PSA
2
3
KLK2
8
6
KLK1
trypsinogen
prostase (KLK-L1)
1
EMSP
4
KLK-L2
7
TLSP

(B)

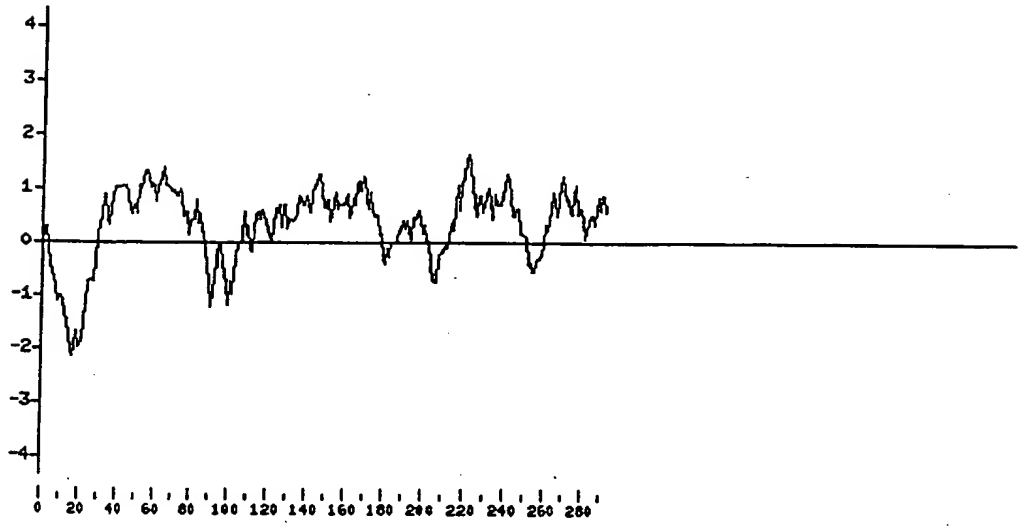

4
3
2
1
0
-1
-2
-3
-4
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280

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FIGURE 11

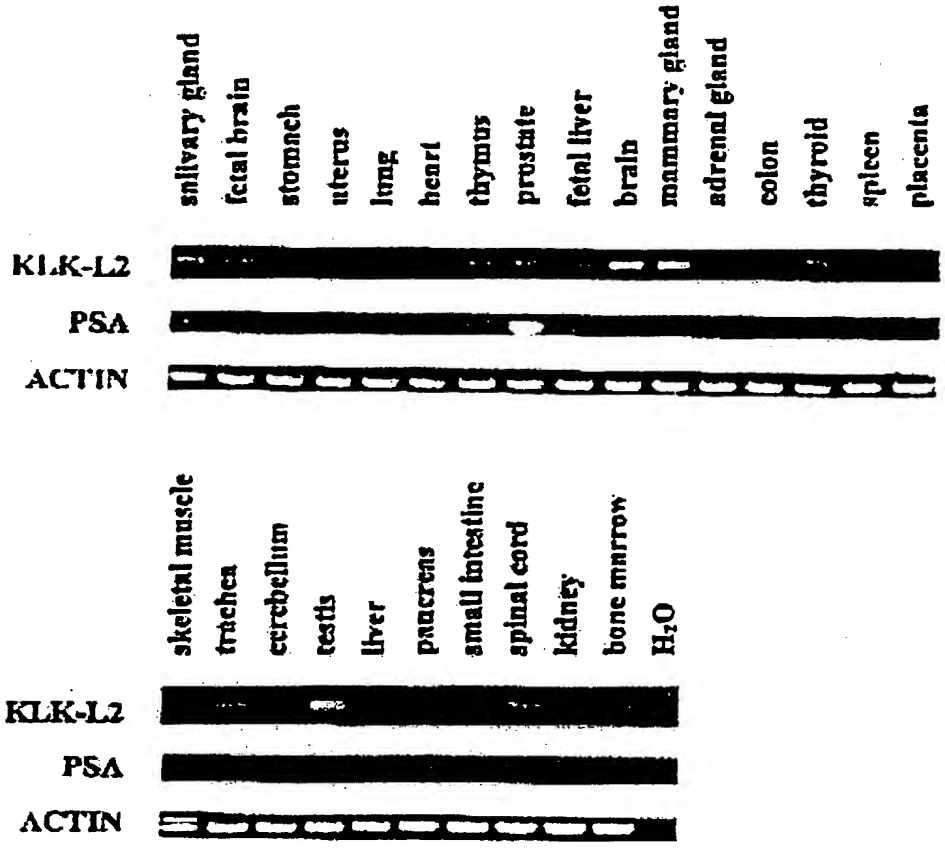

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FIGURE 12

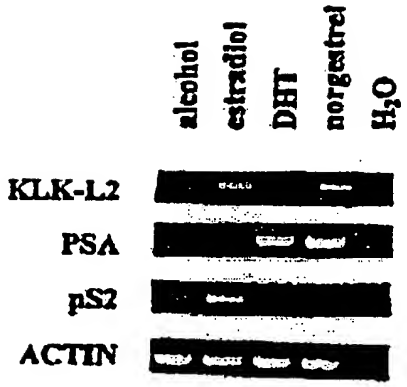

FIGURE 13

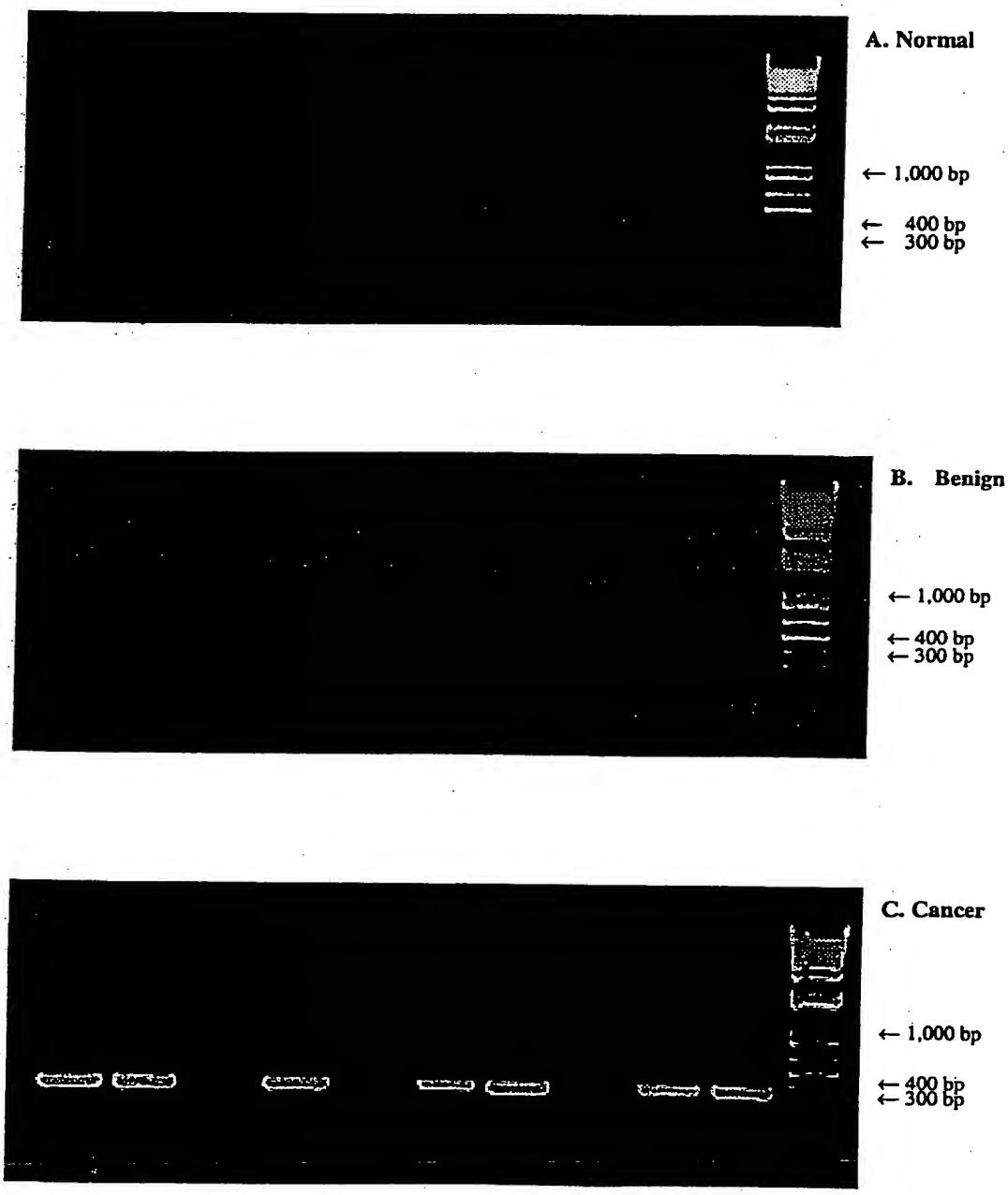
A. Normal
← 1,000 bp
← 400 bp
← 300 bp
B. Benign
← 1,000 bp
← 400 bp
← 300 bp
C. Cancer
← 1,000 bp
← 400 bp
← 300 bp

FIGURE 14

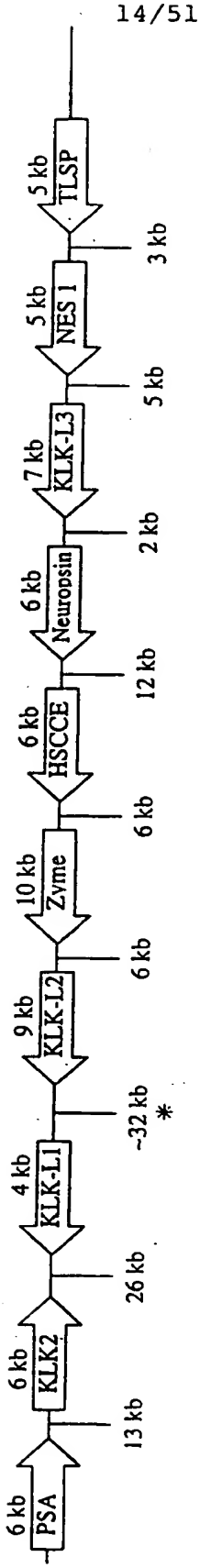
6 kb
PSA
13 kb
6 kb
KLK2
26 kb
4 kb
KLK-L1
~32 kb
*
9 kb
KLK-L2
6 kb
10 kb
Zyme
6 kb
6 kb
HSCCE
12 kb
6 kb
Neurosin
2 kb
7 kb
KLK-L3
5 kb
5 kb
NES 1
3 kb
5 kb
TLSP

FIGURE 15

CACTGGACGGGTGCACGTTCAGGATCCAGGTGCCCAGGGGTCATGAAG CTG GGA
CTC
M K L G L

CTC TGT GCT CTG CTC TCT CTG CTG GCA G gtga... intron 1 ..ccag GG CAT
GGC
L C A L L S L L A G H
G

TGG GCA GAC ACC CGT GCC ATC GGG GCC GAG GAA TGT CGC CCC AAC TCC
CAG
W A D T R A I G A E E C R C N S
Q

CCT TGG CAG GCC GGC CTC TTC CAC CTT ACT CGG CTC TTC TGT GGG GCG
ACC
P W Q A G L F H L T R L F C G A T

CTC ATC AGT GAC CGC TGG CTG CTC ACA GCT GCC CAC TGC CGC AAG
CCgtga.....
L I S D R W L L T A A H C R K P

intron 2 .....gcagG TAT CTG TGG GTC CGC CTT GGA GAG CAC CAC CTC TGG AAA
Y L W V R L G E H H L W K

TGG GAG GGT CCG GAG CAG CTG TTC CGG GTT ACG GAC TTC TTC CCC CAC
CCT
W E G P E Q L F R V T D F F P H P

GGC TTC AAC AAG GAC CTC AGC GCC AAT GAC CAC AAT GAT GAC ATC ATG
CTG
G F N K D L S A N D H N D D I M L

ATC CGC CTG CCC AGG CAG GCA CGT CTG AGT CCT GCT GTG CAG CCC CTC
AAC
I R L P R Q A R L S P A V Q P L N

CTC AGC CAG ACC TGT GTC TCC CCA GGC ATG CAG TGT CTC ATC TCA GGC
TGG
L S Q T C V S P G M Q C L I S G W

GGG GCC GTG TCC AGC CCC AAG G gtat..... intron acag CG CTG TTT CCA
GTC
G A V S S P K A L F P
V

ACA CTG CAG TGT GCC AAC ATC AGC ATC CTG GAG AAC AAA CTC TGT CAC
TGG
T L Q C A N I S I L E N K L C H W

GCA TAC CCT GGA CAC ATC TCG GAC AGC ATG CTC TGT GCG GGC CTG TGG
GAG
A Y P G H I S D S M L C A G L W E

GGG GGC CGA GGT TCC TGC CAG gtga..... intron ..acag GGT GAC TCT GGG
GGC
G G R G S C Q G D S G
G

CCC CTG GTT TGC AAT GGA ACC TTG GCA GGC GTG GTG TCT GGG GGT GCT
GAG
P L V C N G T L A G V V S G G A E

FIGURE 15 (CONT'D)

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CCC TGC TCC AGA CCC CGG CGC CCC GCA GTC TAC ACC AGC GTA TGC CAC TAC
P C S R P R R P A V Y T S V C H Y

CTT GAC TGG ATC CAA GAA ATC ATG GAG AAC TGA
L D W I Q E I M E N

GCCCGCGCGCCACGGGGGCACCTTGGAAGACCAAGAGAGGCCGAAGGGCACGGGGTA
GGGGGTTCTCGTAGGGTCCCAGCCTCAATGGTTCCCGCCCTGGACCTCCAGCTGCCCTG
ACTCCCCTCTGGACACTAAGACTCCGCCCCTGAGGCTCCGCCCCCTCACGGGTCAAGCA
AGACACAGTCGCGCCCCCTCGGAACGGAGCAGGGACACGCCCTTCAGAGCCGTCTCTAT
GACGTCACCGACAGCCATCACCTCCTTCTTGGAACAGCACAGCCTGTGGCTCCGCCCCA
AGGAACCACTTACACAAAATAGCTCCGCCCCTCGGAACTTTGCCCAGTGGGACTTCCCC
TCGGGACTCCACCCCTTGTGGCCCCGCCTCCTTCACCAGAGATCTCGCCCCTCGTGATGT
CAGGGGCGCAGTAGCTCCGCCCACGTGGAGCTCGGGCGGTGTAGAGCTCAGCCCTTGTG
GCCCCGTCCTGGGCGTGTGCTGGGTTTGAATCCTGGCGGAGACCTGGGGGGAAATTGAG
GGAGGGTCTGGATACCTTTAGAGCCAATGCAACGGATGATTTTTCAGTAAACGGGGAAA
CCTCA

FIGURE 16

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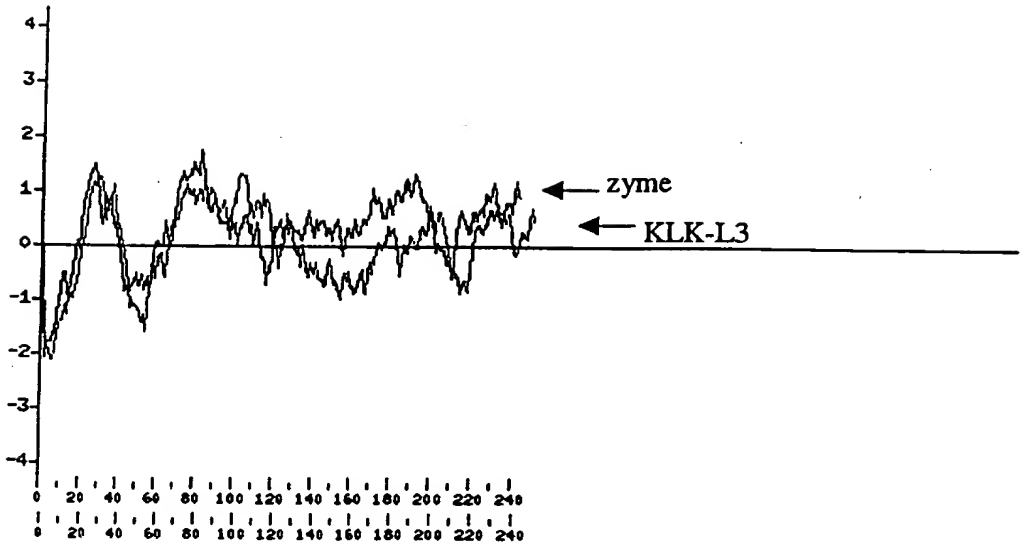


FIGURE 17

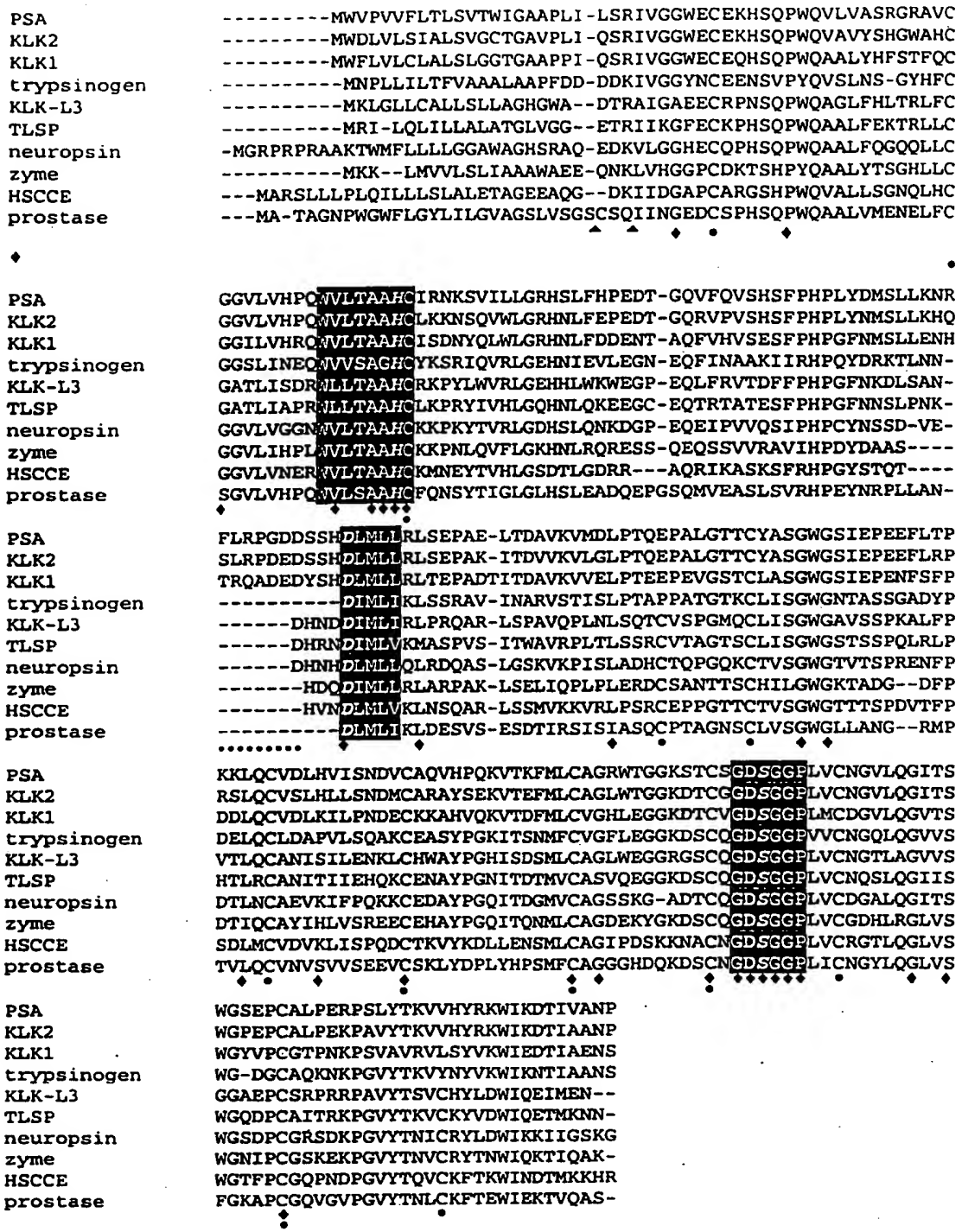

PSA ---------MWVPVVFLTLSVTWIGAAPLI-LSRIVGGWECEKHSQPWQVLVASRGRAVC
KLK2 ---------MWDLVLSIALSVGCTGAVPLI-QSRIVGGWECEKHSQPWQVAVYSHGWAHC
KLK1 ---------MWFLVLCLALSLGGTGAAPPI-QSRIVGGWECEQHSQPWQAALYHFSTFQC
trypsinogen ----------MNPLLILTFVAAALAAPFDD-DDKIVGGYNCEENSVPYQVSLNS-GYHFC
KLK-L3 ----------MKLGLLCALLSLLAGHGWA--DTRAIGAEECRPNSQPWQAGLFHLTRLFC
TLSP ----------MRI-LQLILLALATGLVGG--ETRIIKGFECKPHSQPWQAALFEKTRLLC
neuropsin -MGRPRPRAAKTWMFLLLLGGAWAGHSRAQ-EDKVLGGHECQPHSQPWQAALFQGQQLLC
zyme ----------MKK--LMVVLSLIAAAWAEE-QNKLVHGGPCDKTSHPYQAALYTSGHLLC
HSCCE ---MARSLLLPLQILLLSLALETAGEEAQG--DKIIDGAPCARGSHPWQVALLSGNQLHC
prostase ---MA-TAGNPWGWFLGYLILGVAGSLVSGSCSQIINGEDCSPHSQPWQAALVMENELFC
PSA GGVLVHPQWVLTAAHCIRNKSVILLGRHSLFHPEDT-GQVFQVSHSFPHPLYDMSLLKNR
KLK2 GGVLVHPQWVLTAAHCLKKNSQVWLGRHNLFEPEDT-GQRVPVSHSFPHPLYNMSLLKHQ
KLK1 GGILVHRQWVLTAAHCISDNYQLWLGRHNLFDDENT-AQFVHVSESFPHPGFNMSLLENH
trypsinogen GGSLINEQWVVSAGHCYKSRIQVRLGEHNIEVLEGN-EQFINAAKIIRHPQYDRKTLNN-
KLK-L3 GATLISDRWLLTAAHCRKPYLWVRLGEHHLWKWEGP-EQLFRVTDFFPHPGFNKDLSAN-
TLSP GATLIAPRWLLTAAHCLKPRYIVHLGQHNLQKEEGC-EQTRTATESFPHPGFNNSLPNK-
neuropsin GGVLVGGNWVLTAAHCKKPKYTVRLGDHSLQNKDGP-EQEIPVVQSIPHPCYNSSD-VE-
zyme GGVLIHPLWVLTAAHCKKPNLQVFLGKHNLRQRESS-QEQSSVVRAVIHPDYDAAS----
HSCCE GGVLVNERWVLTAAHCKMNEYTVHLGSDTLGDRR---AQRIKASKSFRHPGYSTQT----
prostase SGVLVHPQWVLSAAHCFQNSYTIGLGLHSLEADQEPGSQMVEASLSVRHPEYNRPLLAN-
PSA FLRPGDDSSHDLMLLRLSEPAE-LTDAVKVMDLPTQEPALGTTCYASGWGSIEPEEFLTP
KLK2 SLRPDEDSSHDLMLLRLSEPAK-ITDVVKVLGLPTQEPALGTTCYASGWGSIEPEEFLRP
KLK1 TRQADEDYSHDLMLLRLTEPADTITDAVKVVELPTEEPEVGSTCLASGWGSIEPENFSFP
trypsinogen ----------DIMLIKLSSRAV-INARVSTISLPTAPPATGTKCLISGWGNTASSGADYP
KLK-L3 ------DHNDDIMLIRLPRQAR-LSPAVQPLNLSQTCVSPGMQCLISGWGAVSSPKALFP
TLSP ------DHRNDIMLVKMASPVS-ITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLP
neuropsin ------DHNHDLMLLQLRDQAS-LGSKVKPISLADHCTQPGQKCTVSGWGTVTSPRENFP
zyme -------HDQDIMLLRLARPAK-LSELIQPLPLERDCSANTTSCHILGWGKTADG--DFP
HSCCE -------HVNDLMLVKLNSQAR-LSSMVKKVRLPSRCEPPGTTCTVSGWGTTTSPDVTFP
prostase ----------DLMLIKLDESVS-ESDTIRSISIASQCPTAGNSCLVSGWGLLANG--RMP
PSA KKLQCVDLHVISNDVCAQVHPQKVTKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITS
KLK2 RSLQCVSLHLLSNDMCARAYSEKVTEFMLCAGLWTGGKDTCGGDSGGPLVCNGVLQGITS
KLK1 DDLQCVDLKILPNDECKKAHVQKVTDFMLCVGHLEGGKDTCVGDSGGPLMCDGVLQGVTS
trypsinogen DELQCLDAPVLSQAKCEASYPGKITSNMFCVGFLEGGKDSCQGDSGGPVVCNGQLQGVVS
KLK-L3 VTLQCANISILENKLCHWAYPGHISDSMLCAGLWEGGRGSCQGDSGGPLVCNGTLAGVVS
TLSP HTLRCANITIIEHQKCENAYPGNITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQGIIS
neuropsin DTLNCAEVKIFPQKKCEDAYPGQITDGMVCAGSSKG-ADTCQGDSGGPLVCDGALQGITS
zyme DTIQCAYIHLVSREECEHAYPGQITQNMLCAGDEKYGKDSCQGDSGGPLVCGDHLRGLVS
HSCCE SDLMCVDVKLISPQDCTKVYKDLLENSMLCAGIPDSKKNACNGDSGGPLVCRGTLQGLVS
prostase TVLQCVNVSVVSEEVCSKLYDPLYHPSMFCAGGGHDQKDSCNGDSGGPLICNGYLQGLVS
PSA WGSEPCALPERPSLYTKVVHYRKWIKDTIVANP
KLK2 WGPEPCALPEKPAVYTKVVHYRKWIKDTIAANP
KLK1 WGYVPCGTPNKPSVAVRVLSYVKWIEDTIAENS
trypsinogen WG-DGCAQKNKPGVYTKVYNYVKWIKNTIAANS
KLK-L3 GGAEPCSRPRRPAVYTSVCHYLDWIQEIMEN--
TLSP WGQDPCAITRKPGVYTKVCKYVDWIQETMKNN-
neuropsin WGSDPCGRSDKPGVYTNICRYLDWIKKIIGSKG
zyme WGNIPCGSKEKPGVYTNVCRYTNWIQKTIQAK-
HSCCE WGTFPCGQPNDPGVYTQVCKFTKWINDTMKKHR
prostase FGKAPCGQVGVPGVYTNLCKFTEWIEKTVQAS-

FIGURE 18

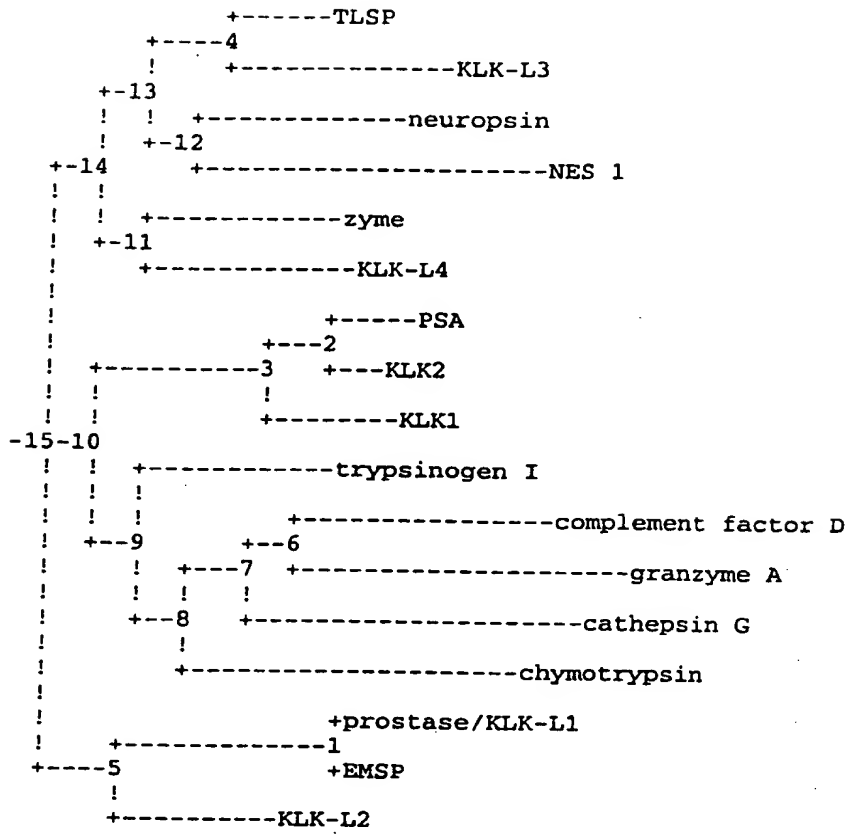

TLSP
4
KLK-L3
13
neuropsin
12
NES 1
14
zyme
11
KLK-L4
PSA
2
3
KLK2
KLK1
15
10
trypsinogen I
complement factor D
9
6
7
granzyme A
8
cathepsin G
chymotrypsin
prostase/KLK-L1
1
5
EMSP
KLK-L2

FIGURE 19

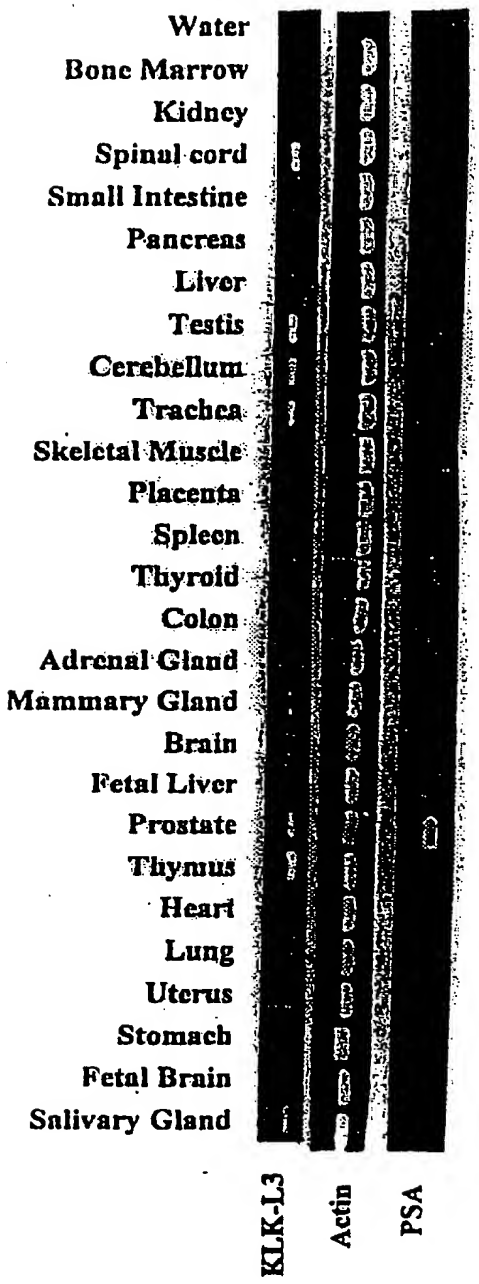

Water
Bone Marrow
Kidney
Spinal cord
Small Intestine
Pancreas
Liver
Testis
Cerebellum
Trachea
Skeletal Muscle
Placenta
Spleen
Thyroid
Colon
Adrenal Gland
Mammary Gland
Brain
Fetal Liver
Prostate
Thymus
Heart
Lung
Uterus
Stomach
Fetal Brain
Salivary Gland
KLK-L3
Actin
PSA

FIGURE 20

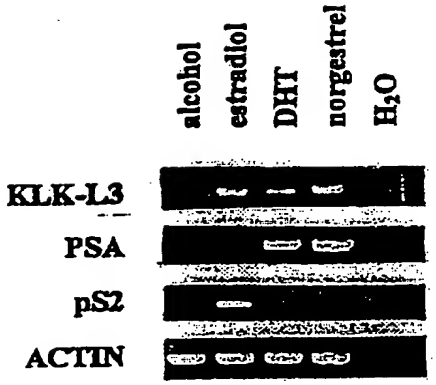


FIGURE 21

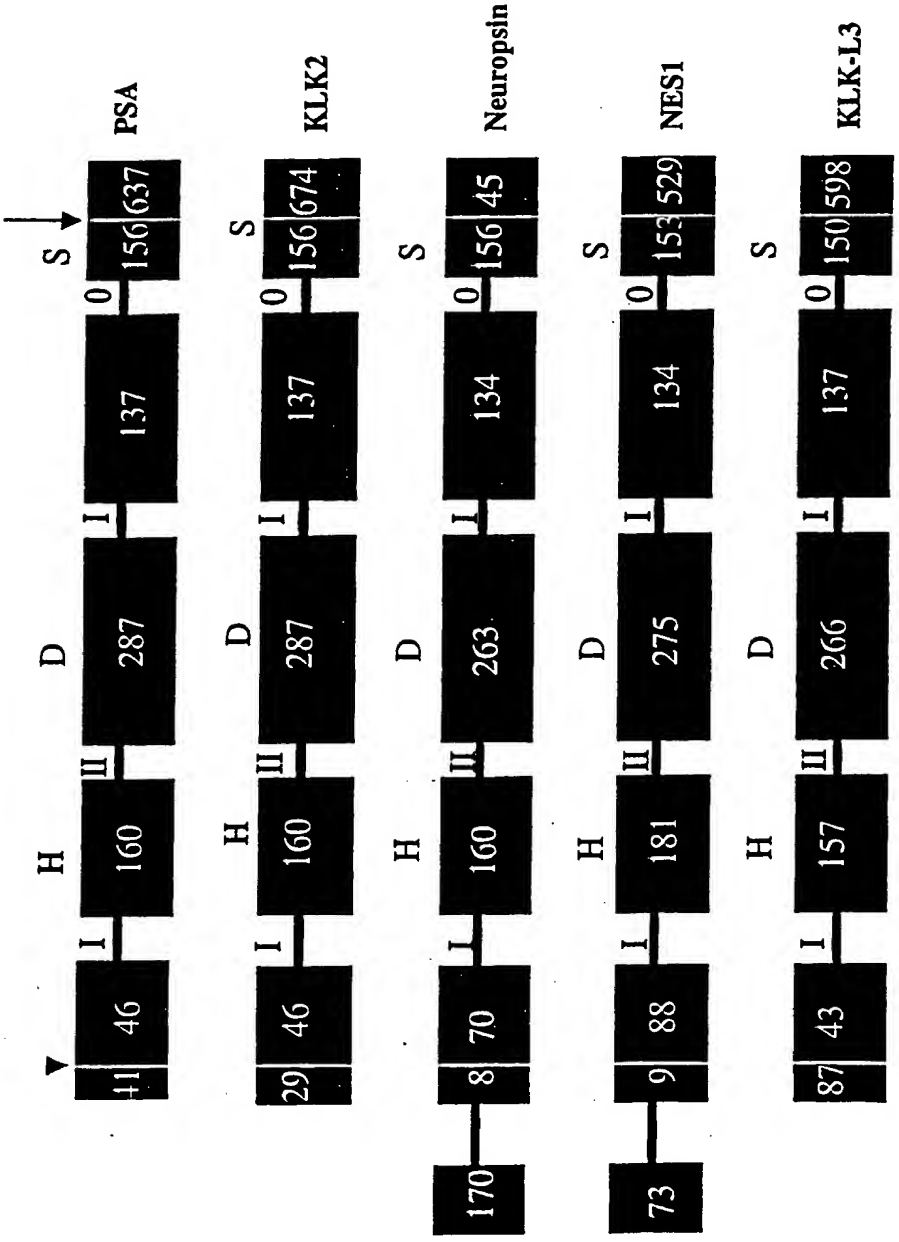

PSA
KLK2
Neuropsin
NES1
KLK-L3
S
H
D
I
II
0
1
41
46
160
287
137
156
637
29
46
160
287
137
156
674
8
70
160
263
134
156
45
170
9
88
181
275
134
153
529
87
43
157
266
137
150
598

FIGURE 22

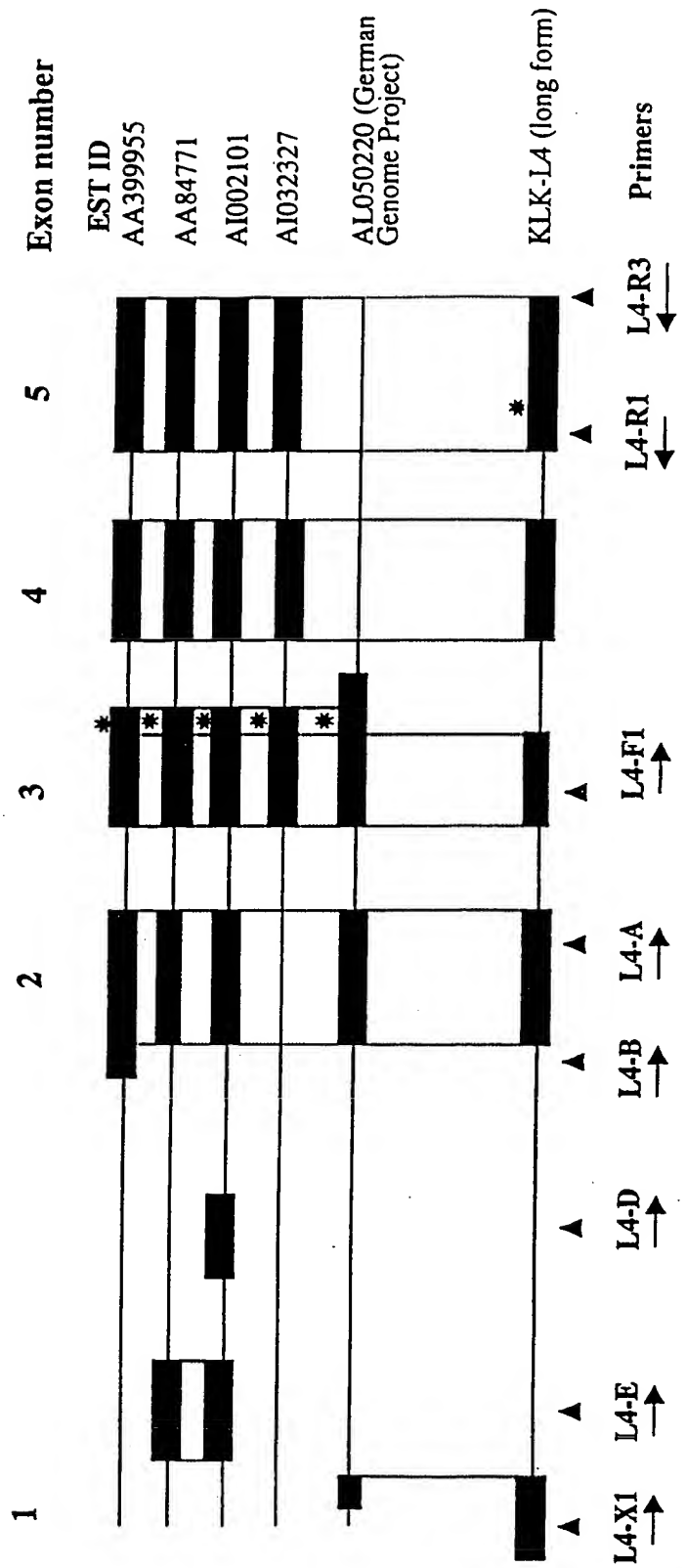

Exon number
EST ID
AA399955
AA84771
AI002101
AI032327
AL050220 (German Genome Project)
KLK-L4 (long form)
Primers
1
2
3
4
5
L4-X1
L4-E
L4-D
L4-B
L4-A
L4-F1
L4-R1
L4-R3

FIGURE 23

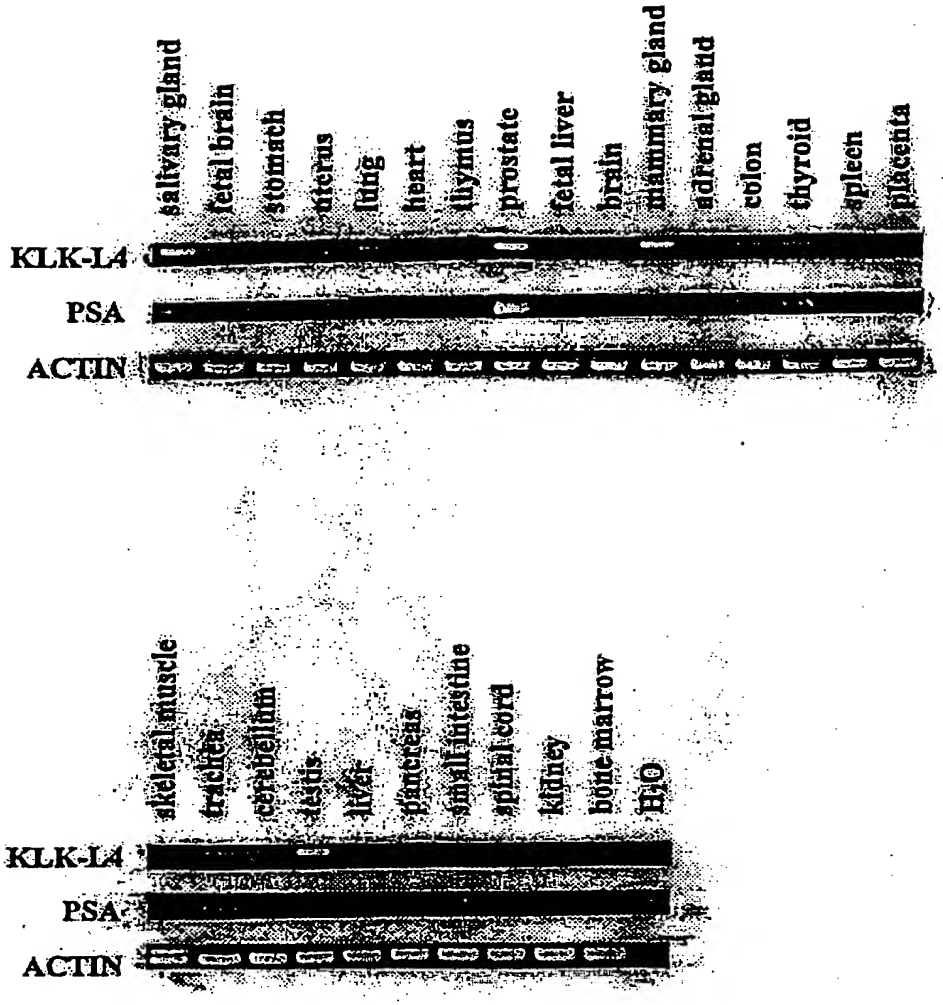

salivary gland
fetal brain
stomach
uterus
lung
heart
thymus
prostate
fetal liver
brain
mammary gland
adrenal gland
colon
thyroid
spleen
placenta
KLK-L4
PSA
ACTIN
skeletal muscle
trachea
cerebellum
testis
liver
pancreas
small intestine
spinal cord
kidney
bone marrow
H2O
KLK-L4
PSA
ACTIN

FIGURE 24

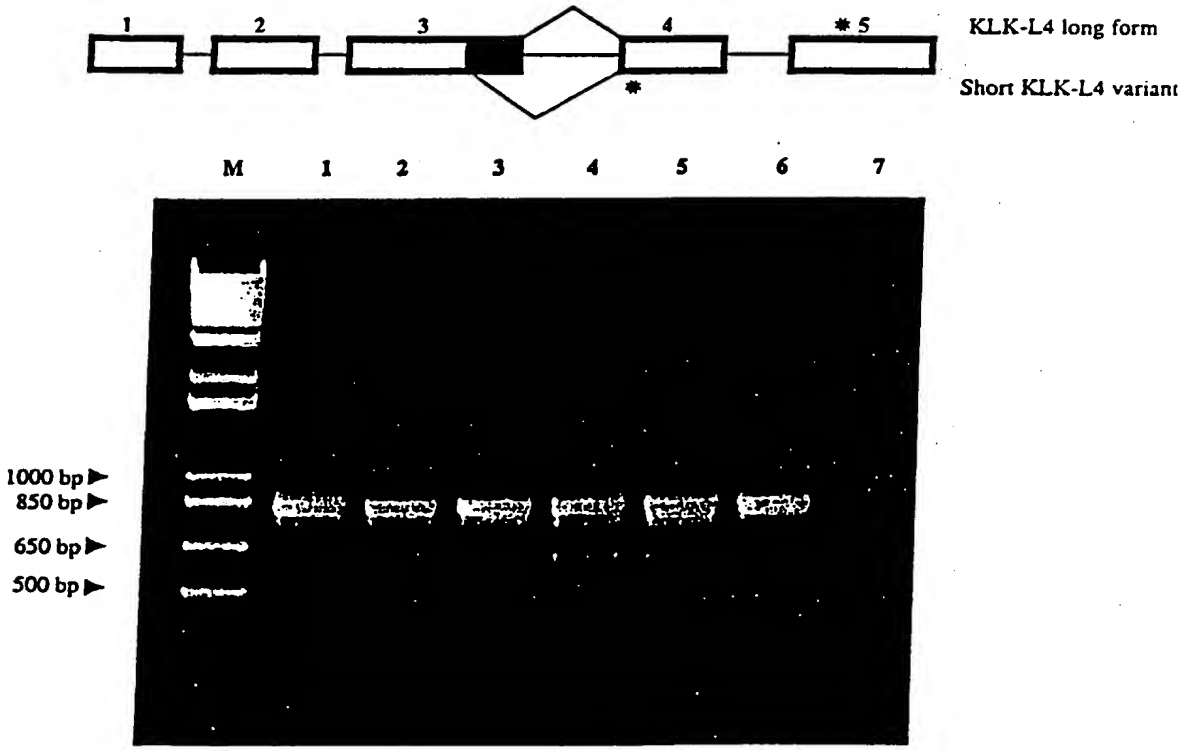

1
2
3
4
* 5
KLK-L4 long form
Short KLK-L4 variant
M
1
2
3
4
5
6
7
1000 bp
850 bp
650 bp
500 bp

FIGURE 25

TCAGGCCCCGCCCGCCCTGCCCTCCCCTCCCGATCCCGGAGCC ATG TGG CCC CTG GCC
M W P L A
CTA GTG ATC GCC TCC CTG ACC TTG GCC TTG TCA GGA G...gtaaga.... intron 1 ..... ttaccag
L V I A S L T L A L S G

GT GTC TCC CAG GAG TCT TCC AAG GTT CTC AAC ACC AAT GGG ACC AGT GGG TTT
G V S Q E S S K V L N T N G T S G F

CTC CCA GGT GGC TAC ACC TGC TTC CCC CAC TCT CAG CCC TGG CAG GCT GCC
L P G G Y T C F P H S Q P W Q A A

CTA CTA GTG CAA GGG CGG CTA CTC TGT GGG GGA GTC CTG GTC CAC CCC AAA
L L V Q G R L L C G G V L V H P K

TGG GTC CTC ACT GCC GCA CAC TGT CTA AAG GA gtatgt ..... intron 2..... cacag G GGG
W V L T A A H C L K E G

CTC AAA GTT TAC CTA GGC AAG CAC GCC CTA GGG CGT GTG GAA GCT GGT GAG
L K V Y L G K H A L G R V E A G E

CAG GTG AGG GAA GTT GTC CAC TCT ATC CCC CAC CCT GAA TAC CGG AGA AGC
Q V R E V V H S I P H P E Y R R S

CCC ACC CAC CTG AAC CAC GAC CAT GAC ATC ATG CTT CTG GAG CTG CAG TCC
P T H L N H D H D I M L L E L Q S

CCG GTC CAG CTC ACA GGC TAC ATC CAA ACC CTG CCC CTT TCC CAC AAC AAC CGC
P V Q L T G Y I Q T L P L S H N N R

CTA ACC CCT GGC ACC ACC TGT CGG GTG TCT GGC TGG GGC ACC ACC ACC AGC
L T P G T T C R V S G W G T T T S

CCC CAG G gtatgcac... intron 3..... tcccc ag TG AAT TAC CCC AAA ACT CTA CAA TGT GCC
P Q V N Y P K T L Q C A

AAC ATC CAA CTT CGC TCA GAT GAG GAG TGT CGT CAA GTC TAC CCA GGA AAG
N I Q L R S D E E C R Q V Y P G K

ATC ACT GAC AAC ATG TTG TGT GCC GGC ACA AAA GAG GGT GGC AAA GAC TCC
I T D N M L C A G T K E G G K D S

TGT GAG gtatgca... intron 4..... aactcag GGT GAC TCT GGG GGC CCC CTG GTC TGT AAC
C E G D S G G P L V C N

AGA ACA CTG TAT GGC ATC GTC TCC TGG GGA GAC TTC CCA TGT GGG CAA CCT
R T L Y G I V S W G D F P C G Q P
GAC CGG CCT GGT GTC TAC ACC CGT GTC TCA AGA TAC GTC CTG TGG ATC CGT
D R P G V Y T R V S R Y V L W I R

FIGURE 25 (CONT'D)

GAA ACA ATC CGA AAA TAT GAA ACC CAG CAG CAA AAA TGG TTG AAG GGC CCA
E T I R K Y E T Q Q Q K W L K G P

CAA (TAA) AAGTTGAGAAATGTACCGGCTTCCATCCTGTCACCATGACTTCCTCAC
Q

ATGGTCTGCTTAGCCCTTCTCTGCTCCTTATTCCCAGTGTTCCATTTGAACCAGTGATCCATGTC
CTGAAAAATGCTCAATCTCAGCTAACATTCCATGTTTCAGAAGCATTCAGGCACTGCCAGGCT
TGCAGTCTCCCAGATGTTGCATCCCTGAAACATCTCAACAACCTGAATGTCCCAACCCAGACA
ATGGCCCAGGTCTCTCAACTTCATCAGTGTGGCTTCTATGAGCCCAGATCACCACCTGAACGT
TCTGTCTGTGGCACATTCTTAAATATTTCCATCAGCCCATCTCAACAATATATGTCCTATAAAT
GGACCATCCTTGACA

FIGURE 26

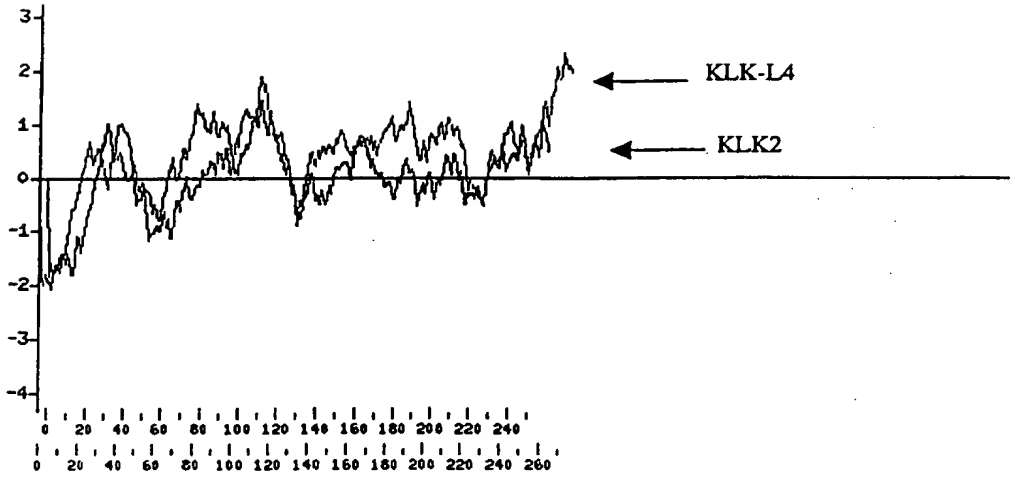
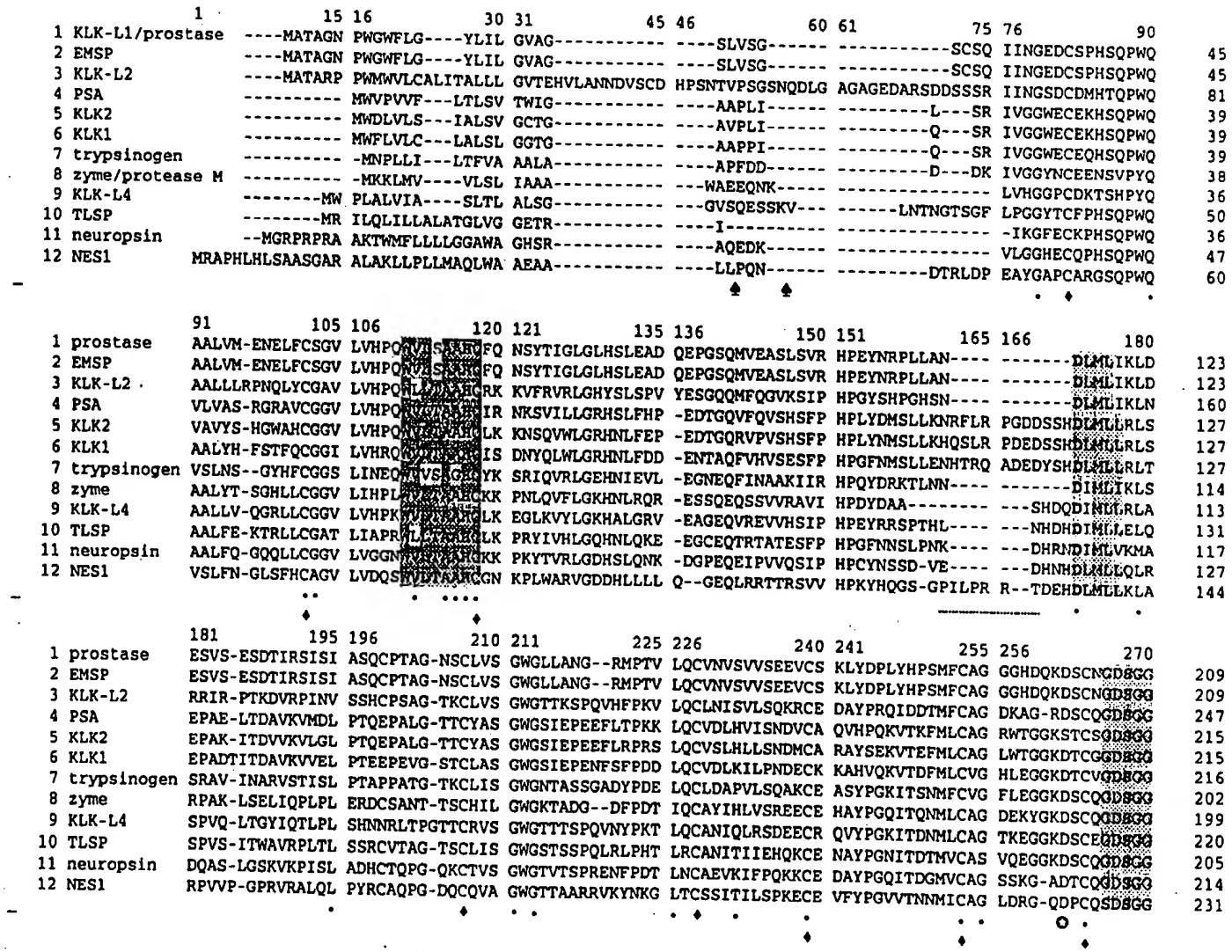
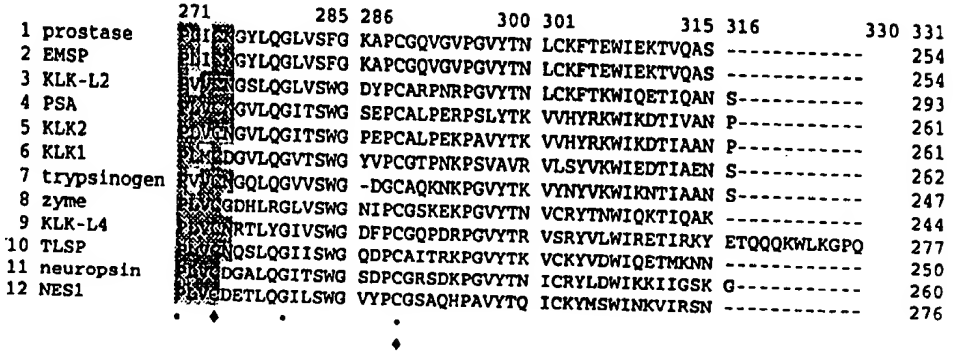

3
2
1
0
-1
-2
-3
-4
KLK-L4
KLK2
0 20 40 60 80 100 120 140 160 180 200 220 240
0 20 40 60 80 100 120 140 160 180 200 220 240 260

FIGURE 27



WO 00/53776
PCT/CA00/00258
29/51
09/936271

FIGURE 27 (CONT'D)



WO 00/53776 PCT/CA00/00258
30/51
09/936271

FIGURE 28

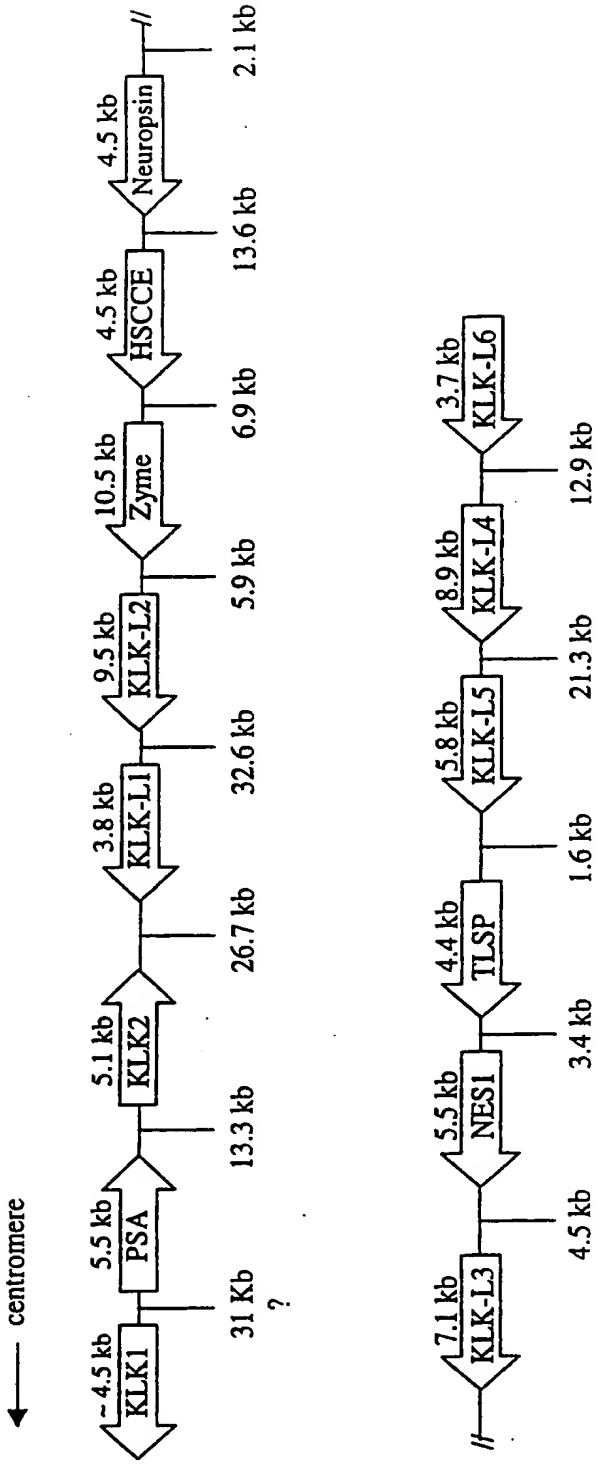

centromere
~4.5 kb
KLK1
5.5 kb
PSA
5.1 kb
KLK2
3.8 kb
KLK-L1
9.5 kb
KLK-L2
10.5 kb
Zyme
4.5 kb
HSCCE
4.5 kb
Neuropsin
31 Kb
?
13.3 kb
26.7 kb
32.6 kb
5.9 kb
6.9 kb
13.6 kb
2.1 kb
7.1 kb
KLK-L3
5.5 kb
NES1
4.4 kb
TLSP
5.8 kb
KLK-L5
8.9 kb
KLK-L4
3.7 kb
KLK-L6
4.5 kb
3.4 kb
1.6 kb
21.3 kb
12.9 kb

FIGURE 29

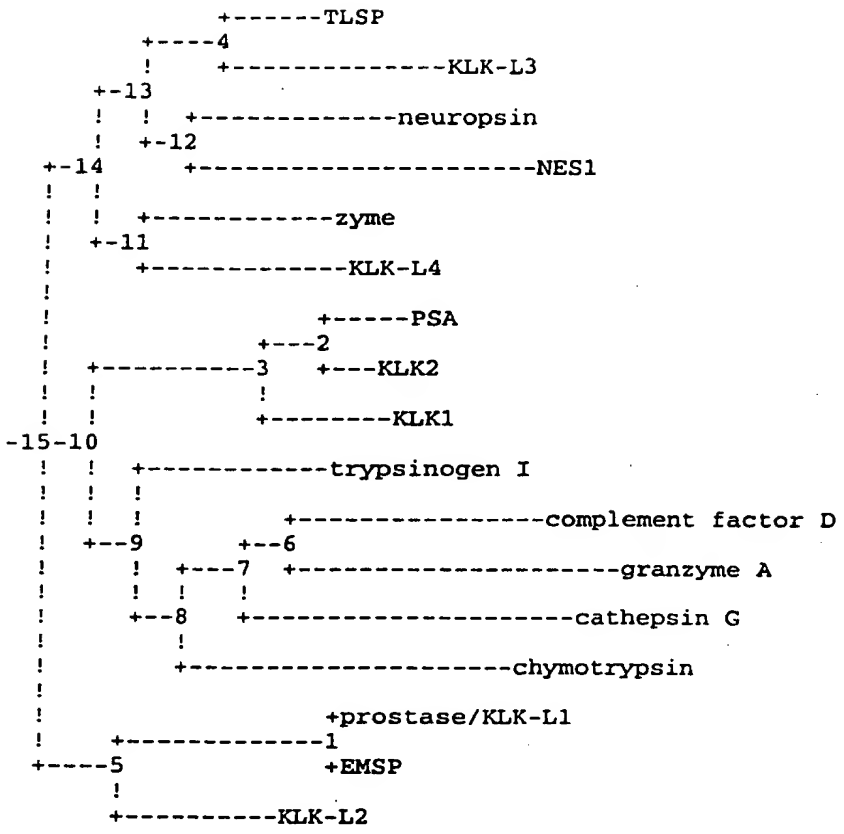

TLSP
4
KLK-L3
13
neuropsin
12
NES1
14
zyme
11
KLK-L4
PSA
2
3
KLK2
KLK1
15
10
trypsinogen I
complement factor D
9
6
7
granzyme A
8
cathepsin G
chymotrypsin
prostase/KLK-L1
1
5
EMSP
KLK-L2

FIGURE 30

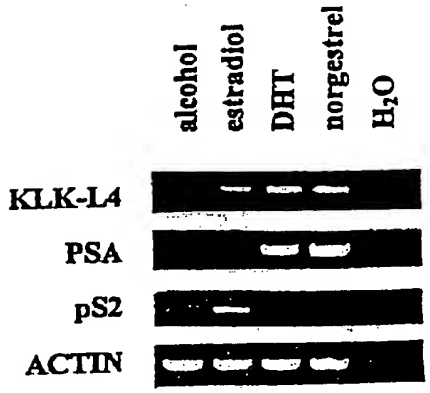


FIGURE 31

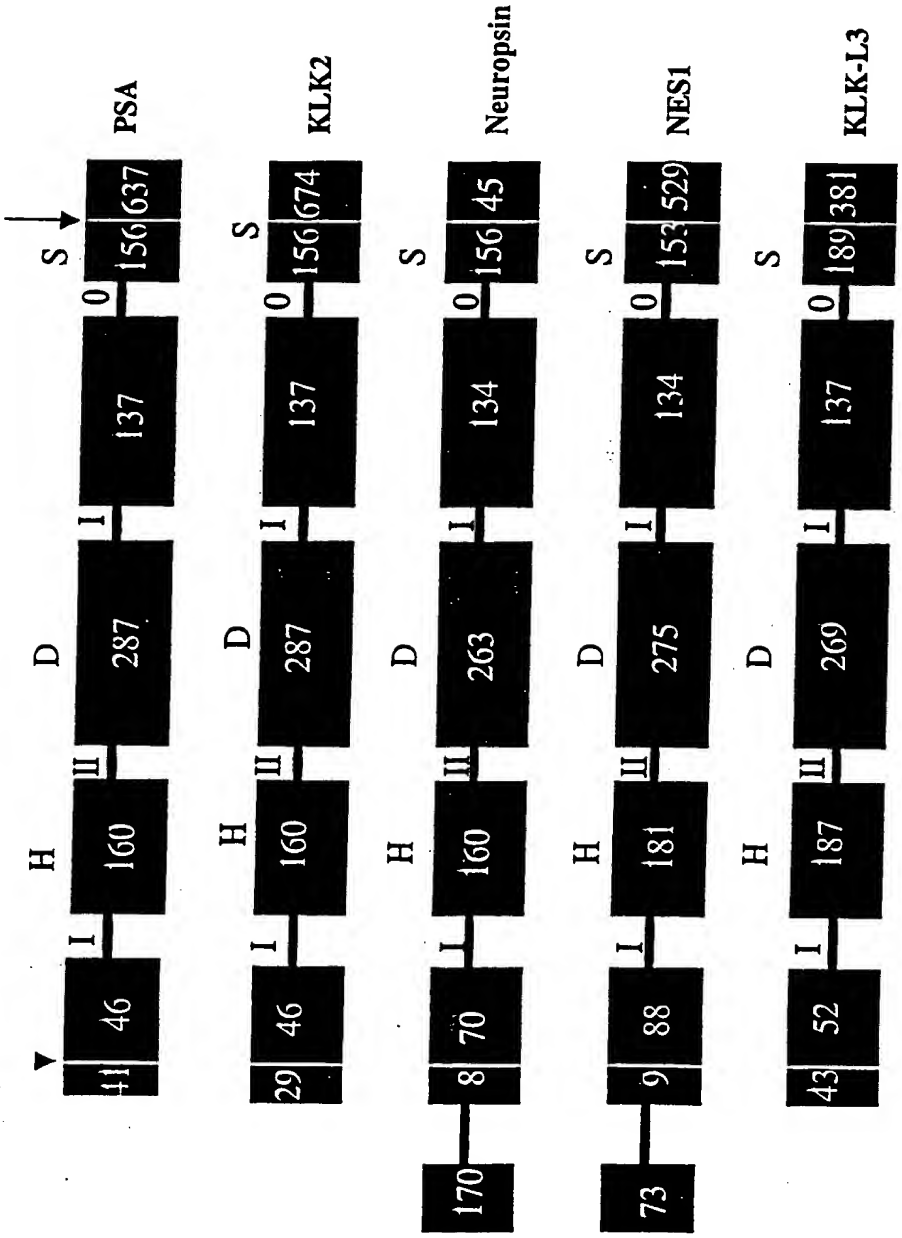

PSA
KLK2
Neuropsin
NES1
KLK-L3
S
D
H
I
II
0
1
41
46
160
287
137
156
637
29
674
170
73
43
52
187
269
189
381

FIGURE 32

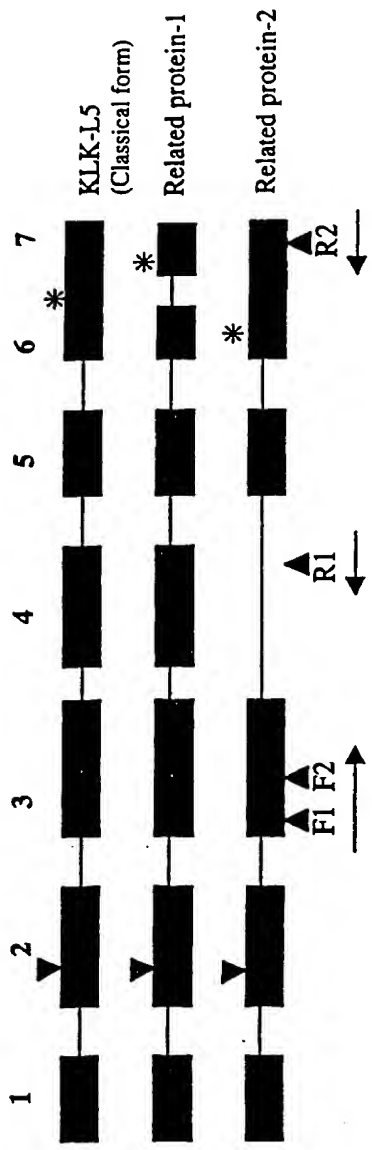

KLK-L5
(Classical form)
Related protein-1
Related protein-2
1
2
3
4
5
6
7
R1
R2
F1 F2

FIGURE 33

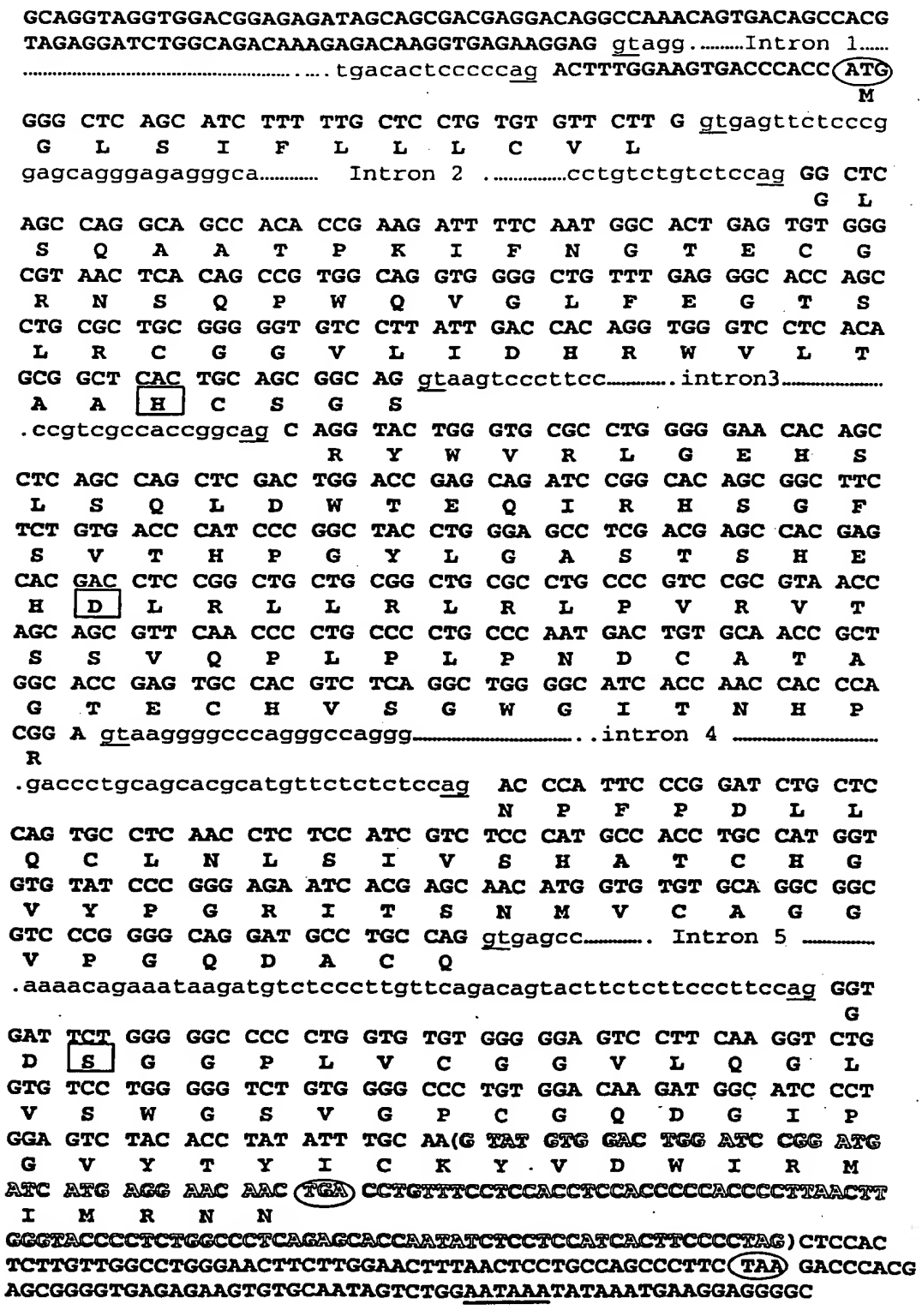

GCAGGTAGGTGGACGGAGAGATAGCAGCGACGAGGACAGGCCAAACAGTGACAGCCACG
TAGAGGATCTGGCAGACAAAGAGACAAGGTGAGAAGGAG gtagg.....Intron 1.....
.....tgacactccccag ACTTTGGAAGTGACCCACC ATG
M
GGG CTC AGC ATC TTT TTG CTC CTG TGT GTT CTT G gtgagttctcccg
G L S I F L L L C V L
gagcagggagagggca..... Intron 2 .....cctgtctgtctccag GG CTC
G L
AGC CAG GCA GCC ACA CCG AAG ATT TTC AAT GGC ACT GAG TGT GGG
S Q A A T P K I F N G T E C G
CGT AAC TCA CAG CCG TGG CAG GTG GGG CTG TTT GAG GGC ACC AGC
R N S Q P W Q V G L F E G T S
CTG CGC TGC GGG GGT GTC CTT ATT GAC CAC AGG TGG GTC CTC ACA
L R C G G V L I D H R W V L T
GCG GCT CAC TGC AGC GGC AG gtaagtcccttcc.....intron3.....
A A H C S G S
.ccgtcgccaccggcag C AGG TAC TGG GTG CGC CTG GGG GAA CAC AGC
R Y W V R L G E H S
CTC AGC CAG CTC GAC TGG ACC GAG CAG ATC CGG CAC AGC GGC TTC
L S Q L D W T E Q I R H S G F
TCT GTG ACC CAT CCC GGC TAC CTG GGA GCC TCG ACG AGC CAC GAG
S V T H P G Y L G A S T S H E
CAC GAC CTC CGG CTG CTG CGG CTG CGC CTG CCC GTC CGC GTA ACC
H D L R L L R L R L P V R V T
AGC AGC GTT CAA CCC CTG CCC CTG CCC AAT GAC TGT GCA ACC GCT
S S V Q P L P L P N D C A T A
GGC ACC GAG TGC CAC GTC TCA GGC TGG GGC ATC ACC AAC CAC CCA
G T E C H V S G W G I T N H P
CGG A gtaaggggcccagggccaggg.....intron 4 .....
R
.gaccctgcagcacgcatgttctctctccag AC CCA TTC CCG GAT CTG CTC
N P F P D L L
CAG TGC CTC AAC CTC TCC ATC GTC TCC CAT GCC ACC TGC CAT GGT
Q C L N L S I V S H A T C H G
GTG TAT CCC GGG AGA ATC ACG AGC AAC ATG GTG TGT GCA GGC GGC
V Y P G R I T S N M V C A G G
GTC CCG GGG CAG GAT GCC TGC CAG gtgagcc..... Intron 5 .....
V P G Q D A C Q
.aaaacagaaataagatgtctcccttgttcagacagtacttctcttcccttccag GGT
G
GAT TCT GGG GGC CCC CTG GTG TGT GGG GGA GTC CTT CAA GGT CTG
D S G G P L V C G G V L Q G L
GTG TCC TGG GGG TCT GTG GGG CCC TGT GGA CAA GAT GGC ATC CCT
V S W G S V G P C G Q D G I P
GGA GTC TAC ACC TAT ATT TGC AA(G TAT GTG GAC TGG ATC CGG ATG
G V Y T Y I C K Y V D W I R M
ATC ATG AGG AAC AAC TGA CCTGTTTCCTCCACCTCCACCCCCACCCCTTAACTT
I M R N N
GGGTACCCCTCTGGCCCTCAGAGCACCAATATCTCCTCCATCACTTCCCCTAG)CTCCAC
TCTTGTTGGCCTGGGAACTTCTTGGAACTTTAACTCCTGCCAGCCCTTC TAA GACCCACG
AGCGGGGTGAGAGAAGTGTGCAATAGTCTGGAATAAATATAAATGAAGGAGGGGC

FIGURE 34

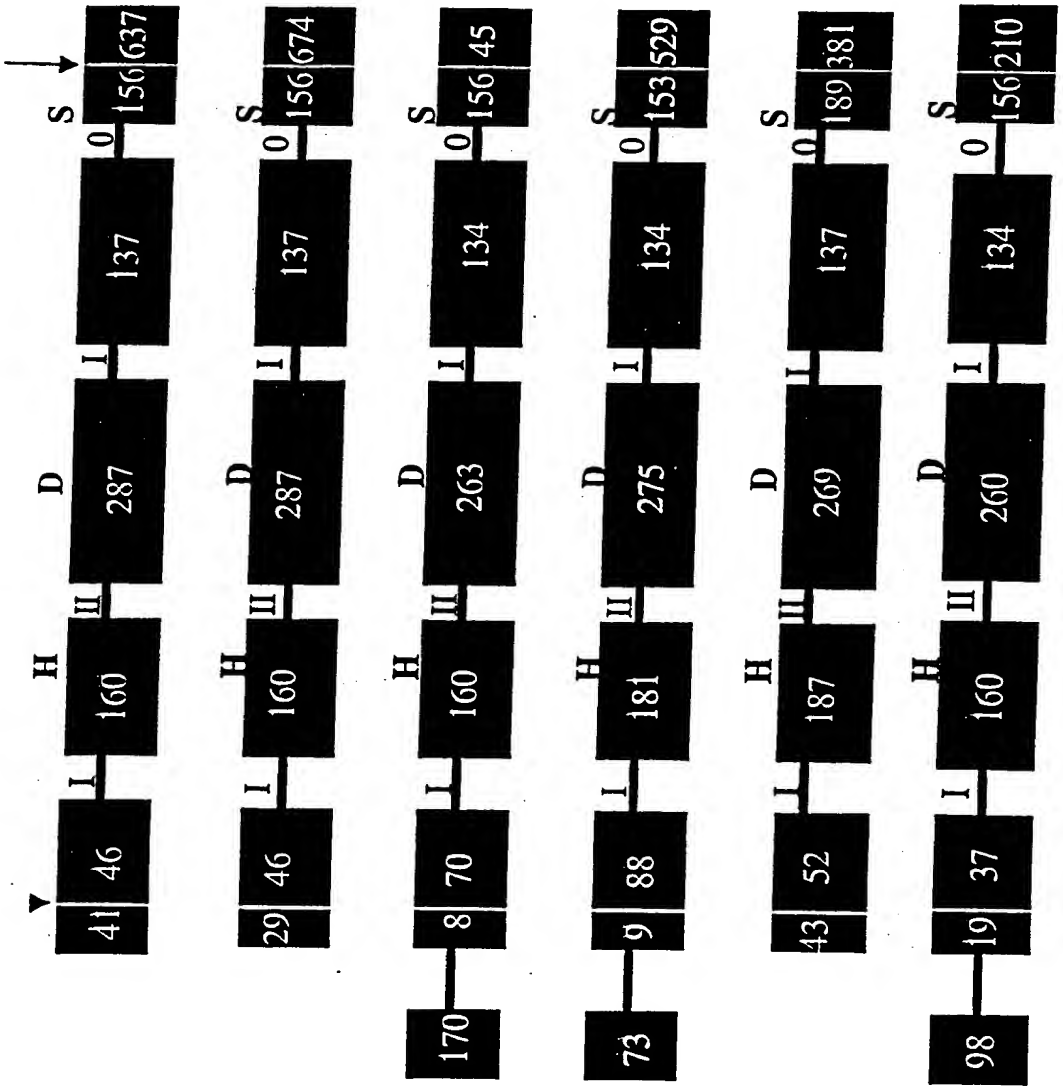

PSA
KLK2
Neuropsin
NES1
KLK-L4
KLK-L5
S
D
H
I
II
III
0
1
41
46
160
287
137
156
637
29
674
8
70
263
134
45
9
88
275
181
529
43
52
187
269
381
19
37
260
210
98
170
73

FIGURE 35

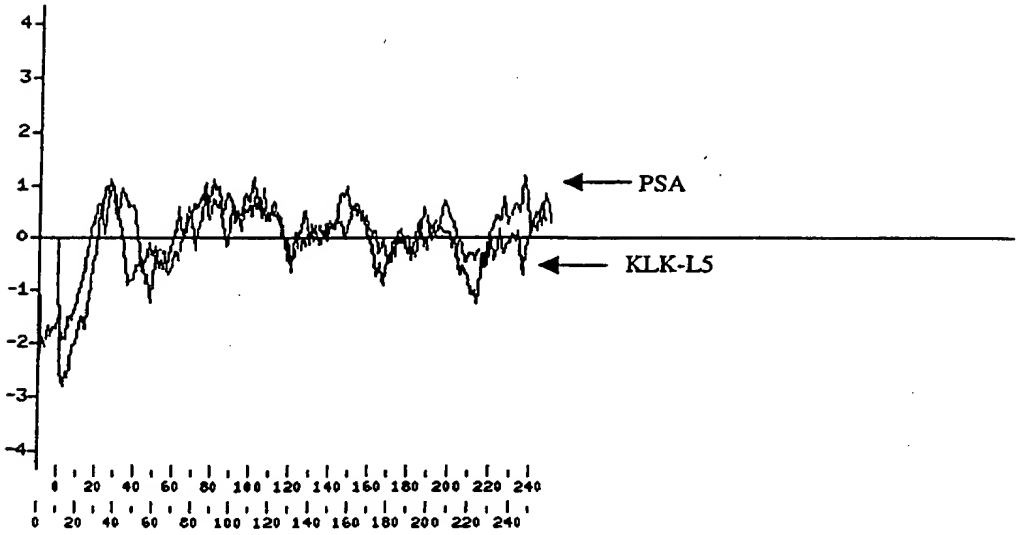

4
3
2
1
0
-1
-2
-3
-4
PSA
KLK-L5
0 20 40 60 80 100 120 140 160 180 200 220 240
0 20 40 60 80 100 120 140 160 180 200 220 240

Figure 36

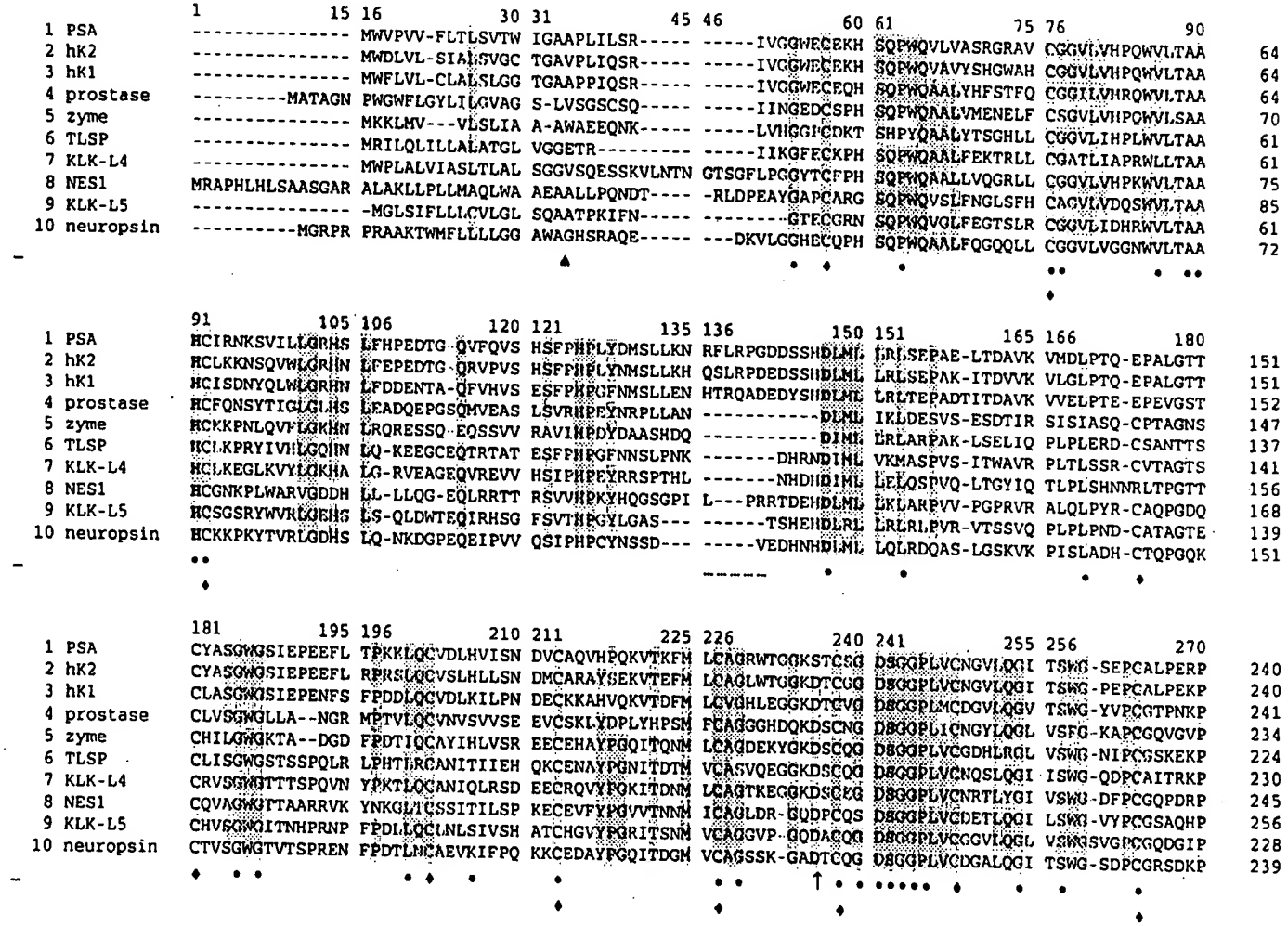

1 PSA
2 hK2
3 hK1
4 prostase
5 zyme
6 TLSP
7 KLK-L4
8 NES1
9 KLK-L5
10 neuropsin

Figure 36 cont'd

```
                271       285 286       300 301
 1 PSA          SLIHKVVHYRKWIKD TIVANP------- --      261
 2 hK2          AVITKVVHYRKWIKD TIAANP------- --      261
 3 hK1          SVAVRVLSYVKWIED TIAENS------- --      262
 4 prostase     GVTTNLCKFTEWIEK TVQAS-------- --      254
 5 zyme         GVTTNVCRYTNWIQK TIQAK-------- --      244
 6 TLSP         GVTTKVCKYVDWIQE TMKNN-------- --      250
 7 KLK-L4       GVTTRVSRYVLWIRE TIRKYETQQQKWLKG PQ    277
 8 NES1         AVTTQICKYMSWIMK VIRSN-------- --      276
 9 KLK-L5       GVTTYICKYVDWIRM IMRNN-------- --      248
10 neuropsin    GVTTNICRYLDWIKK IIGSKG------- --      260
```

FIGURE 37

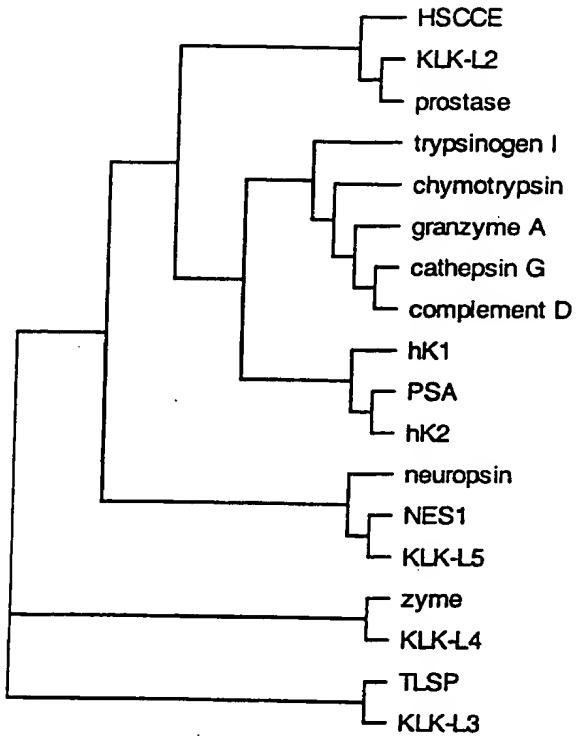

HSCCE
KLK-L2
prostase
trypsinogen I
chymotrypsin
granzyme A
cathepsin G
complement D
hK1
PSA
hK2
neuropsin
NES1
KLK-L5
zyme
KLK-L4
TLSP
KLK-L3

FIGURE 38

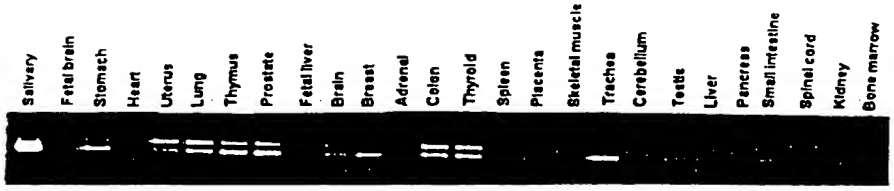

Salivary
Fetal brain
Stomach
Heart
Uterus
Lung
Thymus
Prostate
Fetal liver
Brain
Breast
Adrenal
Colon
Thyroid
Spleen
Placenta
Skeletal muscle
Trachea
Cerebellum
Testis
Liver
Pancreas
Small intestine
Spinal cord
Kidney
Bone marrow

FIGURE 39

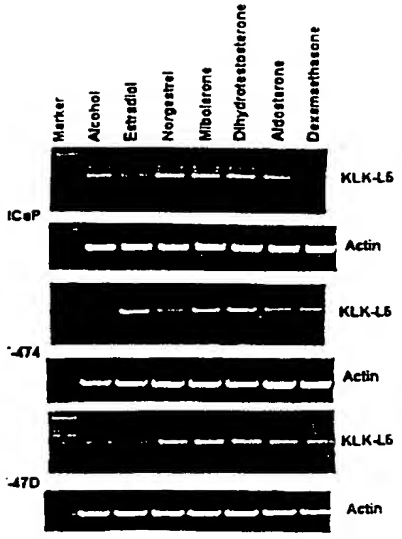

Marker
Alcohol
Estradiol
Norgestrel
Mibolerone
Dihydrotestosterone
Aldosterone
Dexamethasone
KLK-L5
ICaP
Actin
KLK-L5
-474
Actin
KLK-L5
-47D
Actin

FIGURE 40

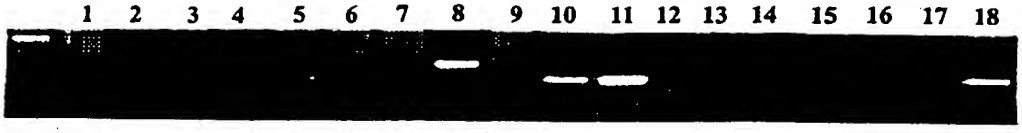


FIGURE 41

ATCGTGTAAT CACCGCCACA TCCAGTGCAA AGCTGATTCG TCACCACAGA GCAGCTCCCT
CCTGCCACCC CATCCCTGGG TCCCAAGAGA ACCCTTTCTT AAAAGAGGGA GTTCTTGACG
GGTGTGGTGG CTCATGCCTG TAATCCTTGC ACTTTGGGAG GCCAAGGAGG GTGGATCATT
TGAGGTCAGG AGTTTGAGAC CAGACTGGCC AACATGGTGA AACCCTGTCT TTACTAAAAA
TACAAAAAAA TGAGCGGGGC ATGGTGGTGG GTGCCTATAG CCCCAGCTAC TCAGGAGGCT
GAGGCAGGAG AATCGCTTGA ACCCAGGAGG CAGAGGTTGC AGTGAGCCGA GATTGAGCCA
CTGCACTCCA GCCGGGGCTA AAGAGTGAGA CTCTGTCTCA AAAAAAAAAA AAAGAAAAAG
AAAAAAAGAA AAAAAAATAA AATAAATAAA TAAATAAAAT AAATTTAAAA ATTTAAAAAT
AAAGAGGGGG TTCTTGTGTT GATGCCGAGC CTGAACCAAG GCAGAGGAGG CCGGGAAGGC
TTCCCAAGGC CTTCAGCTCA AAGCAGGGAG GCCCATAGTT AAACAGAAAC AGTTCAGGAA
TCACAGAAAG GCACCTGGGG AGAGATGGGT GTGTGGCTCC AGATGCAGGT GCCCAGACAG
TGCGTCCCCA GGTGTACAGA CAGACCCAGG CCAAGCTCCA GCTCAAAGAG CCAGCCTAGG
GGGGTGCCGA GGTGGAGGGA GGCTGAGTCA GGCTGAGGCC GGGGAACAGT TGGGGTAGCC
AAGGGAGGCA AGCAGCCTCC TGAGTCACCA CGTGGTCCAG GTACGGGGCT GCCCAGGCCC
AGAGACGGAC ACAAGCACTG GGGAATTTAA GGGGCTAGGG GAGGGGCTGA GGAGGGTAGG
CCCTCCCCCA AATGAGGATG GAACCCCCCC AACTCCAGAA CCCCCCTGCA GGCTGGCCAG
AATCCTTCCC CATCTCATTC ACTCTGTCTC TCCTGCTCTC TGCCGTCTCC TATTTTGAAT
TTCCAACCCC GTCTGTTAAG ACTGTCCTTC TGTCTCTGAA TCTCTGTCCC CTTCTCTTTC
TGGGTCTCTC TCCCTCTCCC TCTGGGTCTC TGTCCCCCTC TCTGGGTCTC TGTCACTCTC
TCTTTGCATC TCCAGCTCTC ACTTTGTCTC T**GCACCTAGC AGATCCCAAG CTGGGGAATG**
CCAGTTCTGG CACCAACCTT CCTGCTCCCT GCTGGGGCCT CTGCTCCCCC ATCTCTCAGG
AGTCGAAAGT GAGAAAGCAA GGTGGGCAGC TCTGCTCCAG GTCCAGGTAT CTCCCGCCCA
CCTCCTGCCC GTCCTCTATC CCACCCCTCC TCTCCATCTC TCCCTGGCGC TGCCATCTCT
CATCTAGGCC TCCGTCTCCT CTGTCATTGT CCCCATCCCC TGTAGGTGCC CATCCTTCCC
GTCTCCCCTC TGCCATCGGC CTGCCTGTCC CATCCTCTTT CTCCCACCAT GTCCCGTTCT
CTTCCACGTC TCATGCCCGC ACTGCCTTCA TCATCATCGC TGTTGTTCTG TGTGTGTTTG
TGGTGAGTGC CGCATGGTGG GGGCGTCTCG GCCTCTCTCC TCTCTCTCCA CTGTTTTCTC
TTTCTGTGTG TCTGTTTCCA TTCTATCTCC ACCTTCTTCC CTCCGTCTTT TGCTTTTCTA
TCTCCACTTC TCCACACCCC TCTCTCCCTG CGTCTCTGTG TCTCCCTCTT CCTCTGTCTT
GTTTTTTTCC CACCGTCTGC CTCTTCTGTT CCCTGTCACA TCCAACTTCC ACCGGTTTCT
CCAGCTCTCT CCTCAGTTCC TTCTCTCATG AGCACACCTG CCTCTGTGCT CGTATTCCTG
GACTCCTCTC TCTCCACTGT CATATCTTCT CATTCATTTT CCCAGTCTCT CTCTGTCTCT
TGCTCTCCCC CTCTCTGTCA CTCTGTCTCT GTCTCTCTCT TTCTCTCTCT CTCTCTGTGT
CTCTCTGTCT GGCTCTCTCT CTGTCTCTCT CTCCATCTCT CTCTCTCTCT CCCCCCCGTC
ACCCTGTCTC TGTCTCTCTC TGTCTGTGTG TCTCTCTGTC TTTCTCTCTC TCCATCTCTC
TCTGTCTCTC TCTCTCTCTC TCTCTCTCTC CCTCTCTCCC TCCTCCCGTG ACTCCCTCTC
TCAGTCCATC TCTTCCTCCC TCTCTCAGCC CCTTCGTGCC CTTTCCTCTG ACACTCCCCA
CCCTGGTTTC CTGACTCCAC CACTAGATCC ACCACCTCCA GCAACTGGGA ACCCTCCCCT
GCCCACCCTG CCCTGGGGTC CCCTCCCAGG ATTCCTTCTA GATTATAGCA TCTTCCCTGG
GCGGGTTCTC ATGAACAATT GTGGCTGCTT TTTTGGCCAG ACAGGGGAGG GAGGGGATGG
GATCAGGGAG TCCTGGAATG GGAACTAGGC AATAAAAAAA AAAAAATGTC AGAAGCAGGG
CGGCGGGAGG TGGGGGCAGG GCCAGCTGTC CTTACCAGGG ATAAAAGGCT TTGCCAGTGT
GACTAGGAAG AGAGACACCT CCCCTCCTTC CTTCATCAAG **ACATCAAGGA GGGACCTGTG**
CCCTGCTCCA CATCCTCCCA CCTGCCGCCC GCAGAGCCTG CAGGCCCCGC CCCCCTCGTC
TCTGGTCCCT ACCTCTCTGC TGTGTCTTCA TGTCCCTGAG GGTCTTGGGC TCTGGGTAAG
TGCCCCTTGC TGTCTCTGCC TCTCAGCCCC CGGTTCTGTT GAAGGTTCCT TCTCTCTCAC
TTTTTCTCTG CATTTGACAG **GACCTGGCCC TCAGCCCCTA AAATGTTCCT CCTGCTGACA**
GCACTTCAAG TCCTGGCTAT AGGTAAGAGA ACGGTTGGGT ATGACACAAG GGGGTCCCCT
GGAGACTCTG AGAAGAGATG GGGATGGGTC CTTGGGGCCC CTGGATGCTC ATGGTGACCT
CATAAGAAAG AGCAGGGAGT GGTTTGGGGG TCATGGTGGG GGAACGTGCT GGAGGCCTAA
ATTCCTAGTT GTGGAGGTGC TAGGGAATTG TGGGGCCGGG GAGAGAGGTG TTTATAAGGT
CTGGTGCAAA ATACATAAGG AATCTTAGGG AACTATTAGG TCCTGAGTGG GTCATAGCAG
AAAGATCACG GGGCTCTACC TGACTGTGTT AGGAAAGAAA CAATGTCAGA AAGATGTTTT
GTTGTCAGAG GGAAGGTGGA GAAGGATGAT GGGATGGCGG GATCGTGGCA TGGGGTGGCG
GGATCGTGGC ATGGGTGTGT GAGGTGGATG GGGGCAAGTG TGGGGCAAGA GATGGCGGAT
CCTTGGGGTC CCACTGAGTG GGAACGTTGG GGAGGAGACA GGGAGGTCCT TGAATGTGTT
GGGGAAGGAC TCATTGGGGG GAAATGTGGC ATATTTCGAG AAGTGATCAC AGAAATTATG
GGAGCATAGA GCTAAGGGTC GTAGATGTAG CAAGGCCCTG GATAAGGTGG CCACGGCACA
AAATAAGAGA TGCTACGGAG GTGACTTGGG AGGTGAGTCA GAAAGCTCTC CGTGCTGGGG

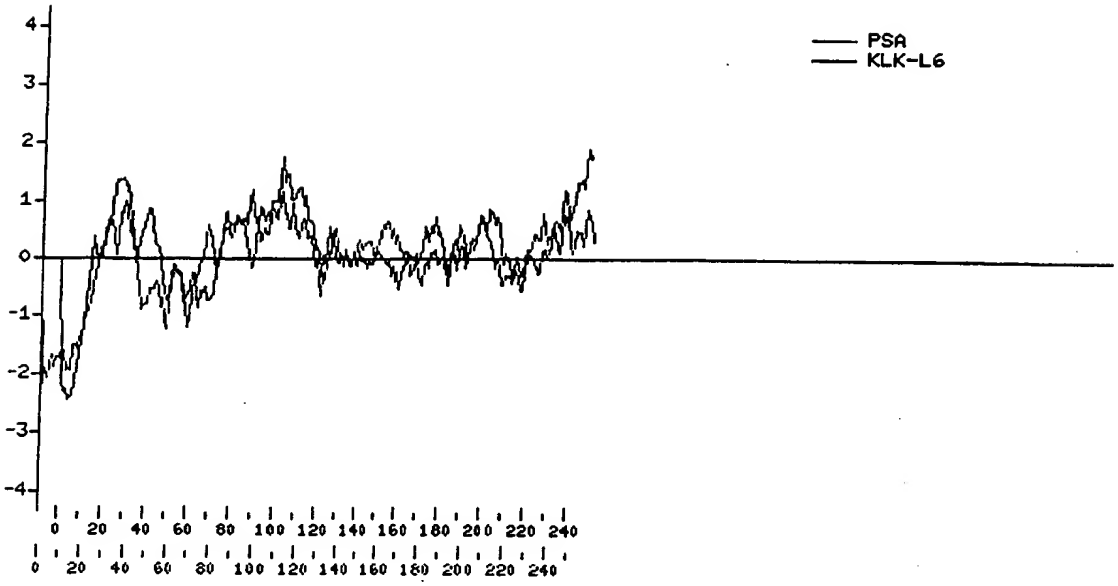
FIGURE 41 (CONT'D)

CAATAACGGG GTCAATATTG GGCATGTCTC ACCCTGGGTG GGACAGATAG AGGCGGGCAG
TTTAGGGGTT AGACCAAAAG GAAGGGGATT TGTCAGTTTT GGAATCCTAC AAACTTGTGG
AGTGGAGAGT GTTTGCTCAT CTACTTTCCC CACCCAATCC TGTCCACTCC TAGCCATGAC
ACAGAGCCAA GAGGATGAGA ACAAGATAAT TGGTGGCCAT ACGTGCACCC GGAGCTCCCA
GCCGTGGCAG GCGGCCCTGC TGGCGGGTCC CAGGCGCCGC TTCCTCTGCG GAGGCGCCCT
GCTTTCAGGC CAGTGGGTCA TCACTGCTGC TCACTGCGGC CGCCCGTAAG TGACCCCCTC
CCCTGTCCCT GTACCTAGTG AATTCCAGAG TCTAAAGCCC TAGAGCTGAG CTGAGAACCT
GGATCTCTGT ATAGAACCCA ATGTAGTGGC TGGCTCCTGG TTTGAGGTCT AGAGAAGAGC
CTGGAACAAA AACACAGCTC GGGATGTGGG CTCCTCCATA AATCTCGAAC TCAGCATAGG
TTCTGAAAGC AGATGGGCAG CTTGGAACCC ATGGACCTGC TGAGAACCGA ACATCTGATC
CAGTGATTCT TCCAGAGGCC ACACATTACA TCGAGACCAA GCTTAGCCCA TTCCAGATTG
GTGGCTGAAT TCAGGACCCC GTCTACATTC AGAAACTCAG GACACTACGT AGAACTCAGA
GCCCAGTTCA GGACCTGCAG TCTAGCCATA AATCCAGAAC TAGAACGCTG CTCACAGCTG
GAACATACAA CTCTAAGAAT AGAGGCAAAA CCTGGAGGCT GTTTCACACC CAAGGTTTAG
TTCAGAGTCT AGTCTATAGC TCCGCTATGA GCAGACTTCA ACCCAGTGTT TGAATCCCAG
AATGTGGCGG GTGCGGTGGC TCATGCCTAT AATCCTAGCA CTTTGGGATG CTGAGGCAGG
CAGATCACCT GAGGTCAGGA GTTCGAGACC AGCCTGAGCA ACATAGAGAA ACCCTGTCTC
TACTAAAAAT GCAAAATTAG CCAGGCATGG TGGCACATGC CTGTAATCCC AGCCACTCGG
GAGGCTGAGG CAGGAGAATC ACTTGAACCT GGGAGGCGGA GGTTGCAGTG AGTCAAGATC
GCACCATTGC ACTCCAGGCT AGGCAACAAG AGCGAAACTC CATATCAATC AATCAATCAA
TAAATCCCAG AATGCAGATC CTAATCAGAA GCCCCATATA AAACCTAGAC CCCTCCTAAA
TTCTAGATCT GAACTTACAA CCCAGACCCC AGCCAAGAGG TCAAAATGCC TATAAGCCAT
ATCTATGCCA TAAACAGGTC AGTCTAGAAC CTAGAGATCA AAGCTCAGGC CAGAGTCTAG
AATATAAAGG CCAGAATGCA AACCAGACTC TAGAATCTTG GATCCGGGCC ATAACCTAGA
GCTCCAACTA GAACCCAGAG CCCAACCTGA GGTCAAGGGC TAGGGCCAGA GTCCAGAACC
AAGAGCCCTA TAATCCAATA TGAAACAGAC CTGTAGAGGC TGGGTGCGGT GGCTCACGCC
TGTAATCCCA GCACTTTGGG AGGCTGAGGC GGGAGAATCA CTTGAACTGG GAGTTGGAGG
TCGAGAGTGA GCTGAGATCG TGCCACTGCA CTCCAGCCTA GGTGACAGAG CGAGACTCCA
TCACAAAAAA AAAATAAATA AATAAATCAA GTCATAATCC AGGTTCGATC TAGAATCCTG
ATCTTAGCAT AGAGTCAAAA GTTTAAGATG TCTAGAACTC AGAACCCAGG CTAGAAACAG
AATGGTGCCT ACTCCGGAAT ATCAGTTCCG ATTTAGAGCC TAGACTCATA ACGCAGTTTC
GCTTAGGACT CAATGCACCG AGCCCAGCAC AGACCCTGGC ACGGAGCCAA GCTCTCCCAA
TCATCACCTT CTTCCCAAGC CAGGAGCTGG AGCCCAGCCC AAGAGCGGAA GGAGAGGCAG
CTGGGGCTGG GCCGAGAGAA TGCCCTGGCC ATGGGGAAGG GCACAGGAGG CCAAGAATGC
TCGGCCTGCA GTTAGTGAGA AGCAGGCTAG ACCTCGGGGA AGACTCGTCA CCCGGCCAGG
GAACCGGGCT GGAGGGTGGG GAGGAGTCTC TGGCTCAGAC CCTGAGCAGC GCTTCTCTTG
GGGGTCGTGG CCAGGATCCT TCAGGTTGCC CTGGGCAAGC ACAACCTGAG GAGGTGGGAG
GCCACCCAGC AGGTGCTGCG CGTGGTTCGT CAGGTGACGC ACCCCAACTA CAACTCCCGG
ACCCACGACA ACGACCTCAT GCTGCTGCAG CTACAGCAGC CCGCACGGAT CGGGAGGGCA
GTCAGGCCCA TTGAGGTCAC CCAGGCCTGT GCCAGCCCCG GGACCTCCTG CCGAGTGTCA
GGCTGGGGAA CTATATCCAG CCCCATCGGT GAGGACTCCT GCGTCTTGGA AAGCAGGGGA
CTGGGCCTGG GCTCCTGGGT CTCCAGGAGG TGGAGCTGGG GGGACTGGGG CTCCTGGGTC
TGAGGGAGGA GGGGCTGGGC CTGGACTCCT GGGTCTGAGG GAGGAGGGGG CTGAGGCCTG
GACTCCTGGG TCTCAAGGAG GAGGAGCTGG GCCTGGACTC ATACGTCTGA GGGAGGAGGG
GCTGGAGCCT GGACTCCTGG GTCTCAAGGA GGAGGGGCTG GGCCTGGACT TCTGGGTCTG
AGGGAGGAGG GGCTGGGGAC CTGGACTCCC GGGTCTGAGG GAGGAGGGAC TGGGGGTCTG
GACTCCTGGG TCTGAGGGAG GAGGGGCTGG GGGCCTGGAC TCCTGGGTCT GAGGGAGGAG
GTGCTGGGGC TGGACTCCTG GGTCGGAAGG AGGAGGGGCT GGGGGCCTGG ACCCTTGGGT
CTTATGGGAG GGTAGACCCA GTTATAACCC TGCAGTGTCC CCCAGCCAGG TACCCCGCCT
CTCTGCAATG CGTGAACATC AACATCTCCC CGGATGAGGT GTGCCAGAAG GCCTATCCTA
GAACCATCAC GCCTGGCATG GTCTGTGCAG GAGTTCCCCA GGGCGGGAAG GACTCTTGTC
AGGTAAGGCC CAGGATGGGA GCTGTGGTAG GGATTATTTG GGACTGGGAT TTAAGCAAAT
GATGTCAGGA GCATGGAAGT CTGCAGAGGT CTTCAGAAGA GAGTGAACCG CAGGCACAGA
GAGATTCCGA TAGCCAGGCC ACCCTGCTTC CTAGCCCTGT GCCCCCTGGG TAATGGACTC
AGAGCATTCA TGCCTCAGTT TCCTCATCTG TCAGGTGGGA GTAACCCTCT TAGGGTAGTT
GGTGGAATGG GATGAGGCAG GTTGGGGAAA GATCGCAGAG TGGCCTCTGC TCATATGGGT

FIGURE 41 (CONT'D)

CTGGGAAAGG CTGTGCTGAG GCTTCTAGAA ATCTTAATGC ATCCTTGAGG GAGGCAGAGA
TGGGGAAATA GAAAAAGAGA GACACACAAA TGTTCTACAG TTGGAGCGAA CAGAGAGGGG
CCTGGTGAGA TTCAAGGGAC AGGCAGGTGC ACACAGAGAC AGAGCCAGAC CCAGCGGAGA
GGGAAGGAAG TGCCCCGACC TCCGGGGCTG AGACCTCAGA GCTGGGGCAG GACTGTGTCC
CTAACTGTCC ACCAGTGTCT CTGCCTGTCT CCCTGTGTCT GCTTCTCGGG TTCTCTGTGC
CATGGTGGCT CTGGCTACCT GTCCATCAGT GTCTCCATTT CTGTTCCTCC CCCTCAGGGT
GACTCTGGGG GACCCCTGGT GTGCAGAGGA CAGCTCCAGG GCCTCGTGTC TTGGGGAATG
GAGCGCTGCG CCCTGCCTGG CTACCCCGGT GTCTACACCA ACCTGTGCAA GTACAGAAGC
TGGATTGAGG AAACGATGCG GGACAAATGA TGGTCTTCAC GGTGGGATGG ACCTCGTCAG
CTGCCCAGGC CCTCCTCTCT CTACTCAGGA CCCAGGAGTC CAGGCCCCAG CCCCTCCTCC
CTCAGACCCA GGAGTCCAGG CCCCCAGCCC CTCCTCCCTC AGACCCGGGA GTCCAGGCCC
CCAGCCCCTC CTCCCTCAGA CCCAGGAGTC CAGGCCCCAG CCCCTCCTCC CTCAGACCCG
GGAGTCCAGG CCCCCAGCCC CTCCTCCCTC AGACCCAGGA GTCCAGGCCC CAGTCCCTCC
TCCCTCAGAC CCAGGAGTCC AGGCCCCCAG CCCCTCCTCC CTCAGACCCA GGAATCCAGG
CCCAGCCCCT CCTCCCTCAG ACCCAGGAGC CCCAGTCCCC CAGCCCCTCC TCCTTGAGAC
CCAGGAGTCC AGGCCCAGCC CCTCCTCCCT CAGACCCAGG AGCCCCAGTC CCCAGCATCC
TGATCTTTAC TCCGGCTCTG ATCTCTCCTT TCCCAGAGCA GTTGCTTCAG GCGTTTTCTC
CCCACCAAGC CCCCACCCTT GCTGTGTCAC CATCACTACT CAAGACCGGA GGCACAGAGG
GCAGGAGCAC AGACCCCTTA AACCGGCATT GTATTCCAAA GACGACAATT TTTAACACGC
TTAGTGTCTC TAAAAACCGA ATAAATAATG ACAATAAAAA TGGAATCATC CTAAATTGTA
TTCATTCATC CATGTGTTTA CTTTTTATTT TTTGAGACAA GGTCTTGCTC AGTCTCCTGG
TGAAATGCTG TAACGCAATC ATAGCTCACT GCAACCGTGA CCTCCTGGGC TCCAGTGATC
CTCTTACCTC AGCCTCCCGA GTAGCTGGGA CCACAGGTGC CCGTCACCAT GCCCCGCTAC
TTTTTAAATT TTGTGTAGAG ATGAGGTTTC CCTGTGTTGC TCAGGCTGGT CTCGAACACC
TGACCCCAAG CAATCCGCCT ACGTCGGTTT CCCAAAGTGC CGGGATTGCA GGCGTGAGCT
GCCGCGCCCA GCCTTATCCA TCCAATTAAT GACTTCAAGA AACATGTACA CAGTGGCCCC
ACCATGCCAA GCCAGGAGCT GTGTACTGAC AAGTGGCTGC CTCCCTCTTT GCGTGTTTTT
CCTTGGGAGT CCCCCGTCCA CCCCACTGTA TCAGGTTTCT AGACGGAAAC ACCTCAGCCC
TGCAGAGTGA CCTTGAGCAT GACTGCCTTC TACCAGCCTC CTCCCTGGAG CCCCTGTGGT
CCAGGGTAGG GAACTAAGTG CCTTGTTTCC TGGAAAATTC TATGCAAATG AAGATGTCCT
CATTTTCCTA ATCAGATCTC AGGTGAGGAG AGTTGAGTTA ATCACAGGCT TCAGTTCCTG
CCCAGGCAAA GCCCTTCTCT CATTTTATTA ATTTATTTCC ACTCTTCATC TCTGGCTCTG
CTCCCCTCCC TCCCCACAGG CACCGACATA AATGGCTTTG AGTGCCCTGC ATCCTTGGAA
AACAAGGCAG TGTCACAGTG TACTGTTTCT AATTTACATG AAACCATTGT GTTAGGAATC
TCATTCTCTT TCTTACTTTC ACTCATCAAC AGCTATTGAG CACCTACTAC GGGCCAGGCA
TTGGTCTATT TATTAGGCAC CTGCTATACA CCAGGCATTG TTCTGGGTGC TGGAGGAAGA
ACTGTGAGCA AGCCAGTCAG AATCCCTGCC CTCACAGAAC TTATATTCTA GCAGGAGATG
ACAGACAAGA AGCCATAAAC ATAATTTTAA AATAAAGCAG AGTCCCTATG AGTAACGAGG
TCAATAAACT TGGGCTGGGC GGCAGGCCCA ATGTGTGCCA GGGCCAGCTC ATACATGCTC
GCAAGAGTCT ACCAGCAAAT TTTCAGGAAT TTCGAGAACC AGTTGCTAAA TGCAGCCATC
ATTAAAAATT AAATTACATA AGCGTATAAT TACATAATTG ATTAAAAAAA TTGTCAGTAA
ATACTCAAAA CTCAACTGTT GCTAATTATT TCAACTAATA CCTATGCTTG GGAGTGAGAT
ATGTCTCTTG TACTACGTCT GTAATGATGA GTTTCTGCAC ACCTCTTTCC AACTCCCCAA
CTCTGTCTGC ACCAGTAGCT TGACAATAGC CAAAGAAGAA GTATTTACTG CACTGAAATT
GAAAAACACT ATAGATAGGG CTTTGCCGGA CAGTCATTGC TAAACCTTTA CCAGGCACCC
TTGGATGGGT CTGCCTGGGA ATGACCTCAT GATCTTAGTG TCTGTCTTCT CAAAGTTCTG
TGCTTGGATA CTGCAGAGTA TAGCTAAAAT AGAATGTTGT ACTCACCTTA TGTTCTATGG
GGACAGCACA GTATTGGGGA ACCCTAAGGT GGCAGGTCTG GGACATGCAC GAAAGATTGC
TGGGAAGTAG AGGCTCCCTC CTTTTCCTCA TCCTCCCACC CCATCCTCCA GTGTCTGGTA
ACCACCATTC TACTCTCTGC TTCTAAGAGT CTGAGTTTTT TAGATTTCAC ATGTAAGTGA
GATCATGCAG TAATTGTCAT TCTGTGTCTG ACCTATTTCA CTTAACACAG TGTCCTCCCG
GTCCATCCAT GTTGTCACAA ATGACAGGAT TTCTTTCTTT TATAAGGCAG AATAATATTA
AATTATACTG ATACTAATAT ATTACATTTC CTTTATCCAT TCATCCATCA ACAGACACAT

FIGURE 42


PSA
KLK-L6
4
3
2
1
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-1
-2
-3
-4
0 20 40 60 80 100 120 140 160 180 200 220 240
0 20 40 60 80 100 120 140 160 180 200 220 240

FIGURE 43

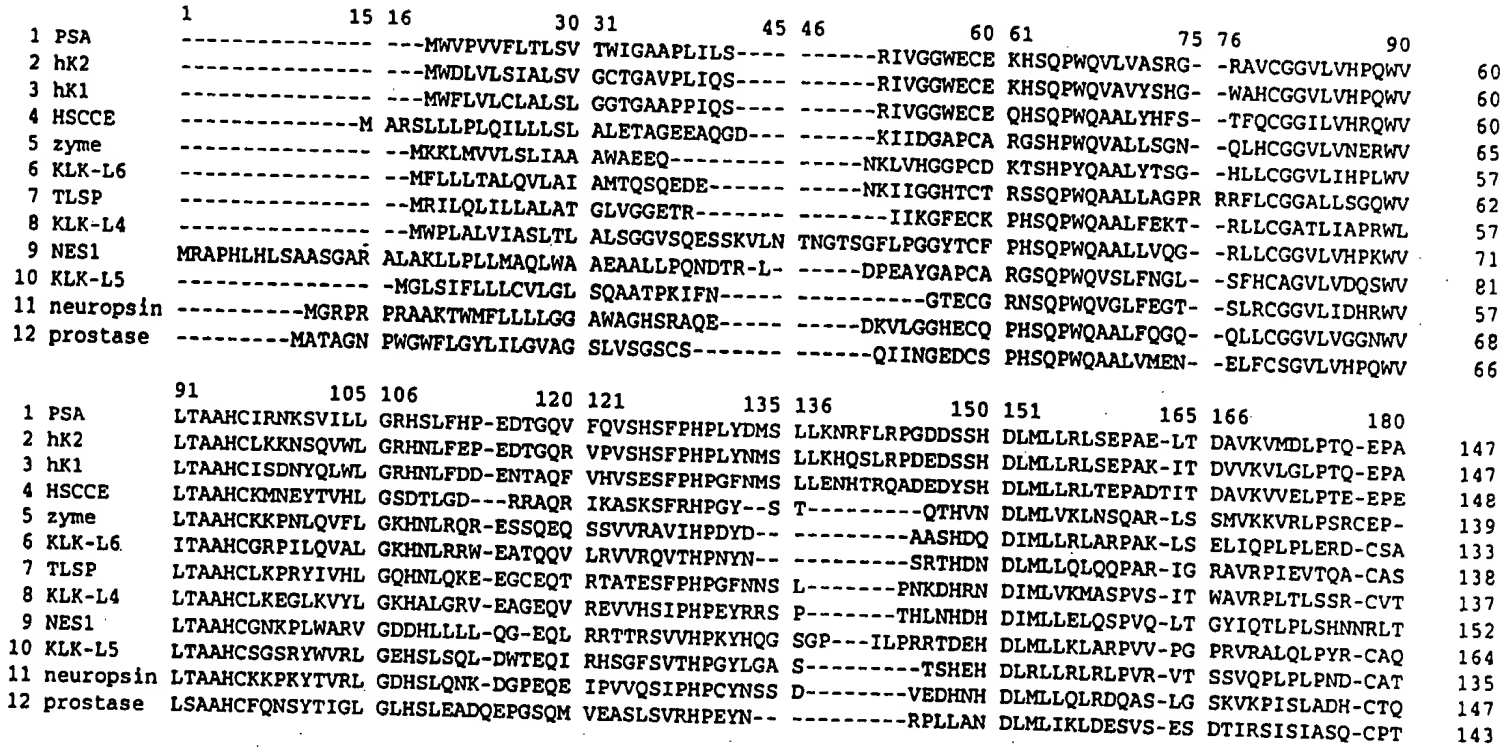
1 PSA
2 hK2
3 hK1
4 HSCCE
5 zyme
6 KLK-L6
7 TLSP
8 KLK-L4
9 NES1
10 KLK-L5
11 neuropsin
12 prostase

FIGURE 43(CONT'D)

```
                181.        195 196         210 211         225 226         240 241         255 256         270
 1 PSA          LGTTCYASGWGSIEP EEFLTPKKLQCVDLH VISNDVCAQVHPQKV TKFMLCAGRWTGGKS TCSGDSGGPLVCNGV LQGITSWG-SEPCAL     236
 2 hK2          LGTTCYASGWGSIEP EEFLRPRSLQCVSLH LLSNDMCARAYSEKV TEFMLCAGLWTGGKD TCGGDSGGPLVCNGV LQGITSWG-PEPCAL     236
 3 hK1          VGSTCLASGWGSIEP ENFSFPDDLQCVDLK ILPNDECKKAHVQKV TDFMLCVGHLEGGKD TCVGDSGGPLMCDGV LQGVTSWG-YVPCGT     237
 4 HSCCE        PGTTCTVSGWGTTTS PDVTFPSDLMCVDVK LISPQDCTKVYKDLL ENSMLCAGIPDSKKN ACNGDSGGPLVCRGT LQGLVSWG-TFPCGQ     228
 5 zyme         NTTSCHILGWGKTAD --GDFPDTIQCAYIH LVSREECEHAYPGQI TQNMLCAGDEKYGKD SCQGDSGGPLVCGDH LRGLVSWG-NIPCGS     220
 6 KLK-L6       PGTSCRVSGWGTISS PIARYPASLQCVNIN ISPDEVCQKAYPRTI TPGMVCAGVPQGGKD SCQGDSGGPLVCRGQ LQGLVSWG-MERCAL     227
 7 TLSP         AGTSCLISGWGSTSS PQLRLPHTLRCANIT IIEHQKCENAYPGNI TDTMVCASVQEGGKD SCQGDSGGPLVCNQS LQGIISWG-QDPCAI     226
 8 KLK-L4       PGTTCRVSGWGTTTS PQVNYPKTLQCANIQ LRSDEECRQVYPGKI TDNMLCAGTKEGGKD SCEGDSGGPLVCNRT LYGIVSWG-DFPCGQ     241
 9 NES1         PGDQCQVAGWGTTAA RRVKYNKGLTCSSIT ILSPKECEVFYPGVV TNNMICAGLDR-GQD PCQSDSGGPLVCDET LQGILSWG-VYPCGS     252
10 KLK-L5       AGTECHVSGWGITNH PRNPFPDLLQCLNLS IVSHATCHGVYPGRI TSNMVCAGGVP-GQD ACQGDSGGPLVCGGV LQGLVSWGSVGPCGQ     224
11 neuropsin    PGQKCTVSGWGTVTS PRENFPDTLNCAEVK IFPQKKCEDAYPGQI TDGMVCAGSSK-GAD TCQGDSGGPLVCDGA LQGITSWG-SDPCGR     235
12 prostase     AGNSCLVSGWGLLAN --GRMPTVLQCVNVS VVSEEVCSKLYDPLY HPSMFCAGGGHDQKD SCNGDSGGPLICNGY LQGLVSFG-KAPCGQ     230

                271         285 286         300 301         315 316         330 331         345 346         360
 1 PSA          PERPSLYTKVVHYRK WIKDTIVANP----- ------ 261
 2 hK2          PEKPAVYTKVVHYRK WIKDTIAANP----- ------ 261
 3 hK1          PNKPSVAVRVLSYVK WIEDTIAENS----- ------ 262
 4 HSCCE        PNDPGVYTQVCKFTK WINDTMKKHR----- ------ 253
 5 zyme         KEKPGVYTNVCRYTN WIQKTIQAK------ ------ 244
 6 KLK-L6       PGYPGVYTNLCKYRS WIEETMRDK------ ------ 251
 7 TLSP         TRKPGVYTKVCKYVD WIQETMKNN------ ------ 250
 8 KLK-L4       PDRPGVYTRVSRYVL WIRETIRKYETQQQK WLKGPQ 277
 9 NES1         AQHPAVYTQICKYMS WINKVIRSN------ ------ 276
10 KLK-L5       DGIPGVYTYICKYVD WIRMIMRNN------ ------ 248
11 neuropsin    SDKPGVYTNICRYLD WIKKIIGSKG----- ------ 260
12 prostase     VGVPGVYTNLCKFTE WIEKTVQAS------ ------ 254
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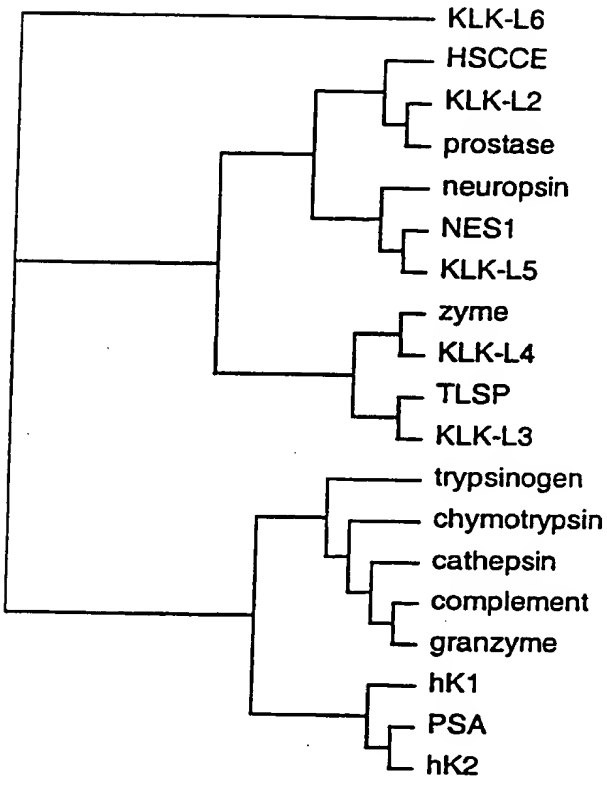
FIGURE 4.4